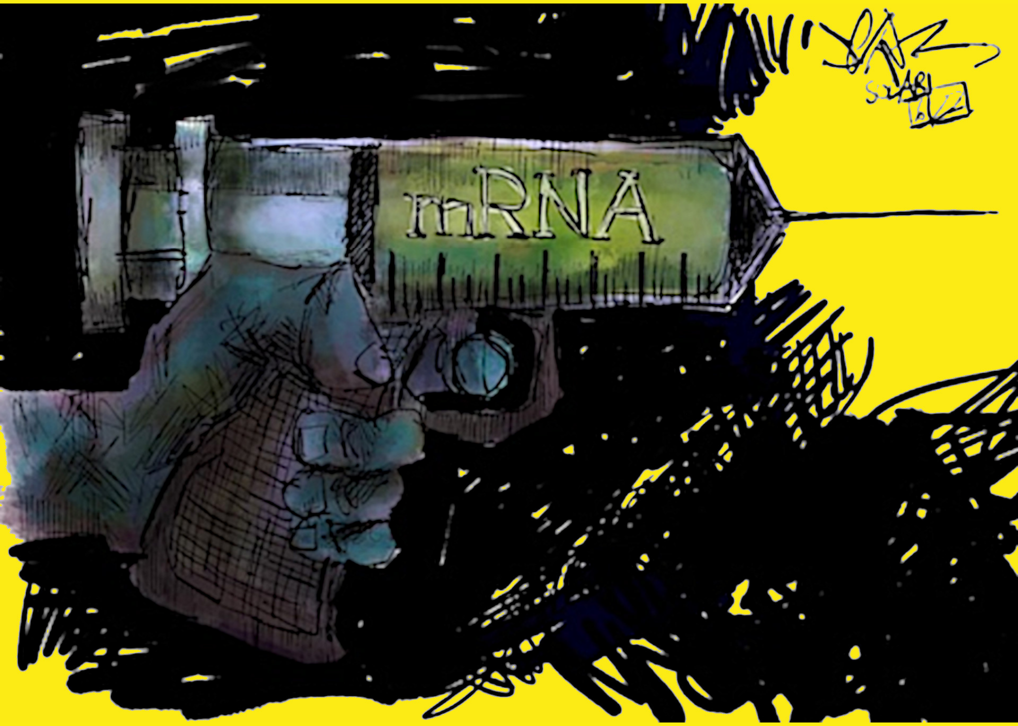
# mRNA Vaccine Toxicity

D4CE.org




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*To the memory of Prof. Arne Burkhardt, MD*

*1944 – 2023*

*Arne was an accomplished pathologist, who in 2021 came out of his well-earned retirement in order to investigate the injury and death caused by the gene-based COVID vaccines.*

*Arne's tireless and expert work provided clear proof of vaccine-induced inflammation in blood vessels and in all major organs. Shortly before his death, Arne had presented his findings at the European Parliament in Brussels.*

*We are deeply grateful to Arne for his dedication, his courage, and his kindness. He will be in our hearts forever.*

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## Foreword

Mary S. Holland, President and General Counsel (on leave), Children's Health Defense

Anyone alive today may be forgiven for experiencing PTSD (Post-Traumatic Stress Disorder) about all things COVID—the lockdowns, the fear mongering, the masking, the testing, the censorship, the suppression of effective treatments, the coerced experimental gene-based shots, and the pervasive injuries and deaths. After three years of horror, it is only human to want to put this behind us and to forget. Yet this book makes abundantly clear that we would do so at our own peril. This undeclared war against humanity is not over, and we must arm ourselves with knowledge.

The book's purpose is to explain what the COVID-19 mRNA vaccine toxicity means for future mRNA vaccines. It outlines three potential mechanisms that likely account for what's happened: (1) the toxicity of the lipid nanoparticles; (2) the toxicity of the vaccine-induced spike proteins; and (3) the immune system's response to them. It concludes that the immune system's response to the spike proteins is the most significant toxic factor because it both corresponds to the autopsy findings of inflammation and immune system damage and jibes with the theoretical mechanisms of harm.

The book's conclusion is bleak: *"Every future mRNA vaccine will induce our cells to produce its own specific antigen, related to the particular microbe it targets. We must therefore expect each such vaccine to induce immunological damage on a similar scale as we have witnessed with those directed against COVID-19."* Recognizing that myriad mRNA vaccines are in the pipeline or already on the market—against flu, RSV, HIV, malaria, cancer, allergies, heart disease, to name a few—this knowledge is as chilling as it is critical.

The book warns: "First and foremost, we must accept that we are indeed in our governments' cross hairs. Instead of relying on their treacherous and malevolent guidance, we must therefore watch out for ourselves and our loved ones—do our own research and seek out honest health advice wherever it may be found, be it inside or outside the established venues of science and of medicine."

You hold in your hands an indispensable primer. The book is comprehensive, drawing on a wide array of published scientific literature, reasonably short and highly readable—156 pages of text and 20 pages of citations—providing required reading on virology, immunology and toxicology. It has excellent citations, illustrations of viral and immune mechanisms, and stained tissue photographs of those who died from COVID-19 shots.

The chapter on the epidemiology of COVID-19 mRNA vaccine adverse events is illuminating—looking at the vast harms to date. Here we learn that 13 billion COVID vaccine doses have been administered worldwide—almost two doses for each person on the planet. And the US dispensed 650 million doses, causing millions of adverse events. The types of injuries are remarkable for their breadth—including myocarditis, blood clotting throughout the body and neurological, immunological and reproductive harms. Still, the CDC has the audacity to call the vaccines "safe" and to recommend them for all people 6 months and up on at least an annual basis.

The final chapter by David Rasnick chronicles how AIDS and HIV became the "blueprint for the perversion of medical science" that we continue to live through today. In the 1980s, Dr. Tony Fauci initiated "science by press release," proclaiming and enforcing an entirely unproven AIDS narrative. Rasnick cogently explains that the AIDS orthodoxy is false, having never been proven despite 40 years and billions of dollars invested. He writes:

> *[A]s incredible as this may sound, there has not been a single scientific study designed or conducted to determine whether or not AIDS—or even HIV—is sexually transmitted. . . .*
>
> *Since WWII—but especially in recent decades—the stifling of debate and the persecution of dissenters has become entrenched in virtually every major field of science in the US. It is particularly virulent in the so-called biomedical sciences. . . .*

*The conjoining of government, big business and academe which President Eisenhower warned about in 1961 now rules the world. … The COVID-19 fraud is the AIDS scam writ large. … We are in the middle of a global totalitarian takeover and things are going to get much worse in the months ahead.*

The book's overall conclusion echoes Rasnick:

*It is not possible to interpret the actions of the authorities as "honest mistakes." Too much has occurred that points unequivocally to a sinister agenda behind the gene-based COVID-19 vaccines. The rushed approval without necessity, the outright threats and the coercion, the systematic censorship of honest science and the suppression of the truth about the numerous killed or severely injured vaccine victims have all gone on for far too long to permit of any doubts as to intent and purpose. Our governments and the national and international administrative bodies are waging an undeclared war on all of us … [T]his war has been going on for decades, and we must expect it to continue and to escalate.*

While this well-founded information is both alarming and depressing, knowledge is power. If we come to grips with the reality that past and future harm from mRNA vaccines is both intentional and inevitable, we can protect ourselves and our loved ones. Forewarned is forearmed. Read this book and keep it close as a reference until we've turned the page on this dark chapter in global history.

# Preface

The purpose of this book is to examine and understand the damage caused by the COVID-19 mRNA vaccines, and to draw from this analysis the right lessons concerning the use of mRNA vaccines against infectious diseases in general. We make the case that, in spite of a conspiracy of silence and censorship in the media and much of the scientific establishment, the damage done by the COVID-19 mRNA vaccines is now clear beyond doubt. This assessment is supported both by statistical evidence and by pathological findings on autopsy and biopsy materials from vaccine victims. The statistical aspects are addressed in Chapter 7, contributed by Children's Health Defense researchers Margot DesBois and Brian Hooker. Chapter 4 on pathology is based in part on the peer-reviewed literature, but to a significant extent also on the work of Arne Burkhardt, a very senior pathologist from Germany, who made his as yet unpublished findings on the autopsy materials of numerous vaccine victims available to us. Unfortunately, Arne was torn from us, and from his ongoing work, by his unexpected passing on May 30, 2023. We are deeply saddened, but at the same time deeply grateful for his outstanding and crucially important contributions.

From our analysis of both statistical data and pathological findings, we infer that the experience with these vaccines presages similar levels of danger and damage with future mRNA vaccines, regardless of the particular microbial antigen or antigens they may encode. In order to make our reasons understandable to non-specialists, we prefix our exploration of the evidence with an introduction to some basic aspects of immunology (Chapter 2), as well as to the interactions between mRNA vaccines and the immune system (Chapter 3).

One of the most striking lessons of the last three years is the degree of rot and subversion of medicine in all its aspects—medical science, clinical medicine, and public health. The recent events in this category would certainly have warranted discussion here as well. However, much

has already been said about this subject by others. Therefore, we chose instead to provide a historical perspective, in the form of David Rasnick's piece on AIDS and HIV in Chapter 8. David makes a strong case that the manipulations that we have seen with COVID had already been used decades ago to force flawed science and outright lies on an unsuspecting public, and harmful treatments on those declared the carriers of this supposedly deadly viral infection.

It is often said that in war truth is the first casualty. In the COVID era, many of us have woken up to the war on the people that is being waged using deceptive science and harmful "public health" measures. David's chapter makes it clear that this war has been going on for a long time. We therefore must expect that it will continue. With this book, we want to help you to protect yourself and your loved ones from such premeditated attacks on your health, your lives, and your liberty.

# 1. Introduction

The COVID-19 mRNA vaccines were the first application of mRNA technology for the stated purpose of immunization against an infectious disease. However, mRNA vaccines against a number of other infectious agents are already in the works [1]. The purpose of this book is to help you understand the effects that such future vaccines would likely have on your health. While the available evidence is so far limited to the COVID-19 vaccines, the patterns of injury observed with these point to fundamental problems that must be expected to recur with future mRNA against other pathogens.

## 1.1 Are mRNA vaccines dangerous in principle, or is the observed harm accidental?

The facts presented in this book will make it clear that the COVID-19 mRNA vaccines have done very significant harm. We might wonder whether this damage was caused by these vaccines working as intended, or rather by undeclared ingredients or contaminants. This question cannot be dismissed out of hand. Several kinds of contaminations have been clearly documented; and furthermore, there is an unusually large spread in the rate of adverse events between batches of the same COVID-19 vaccines, which indicates at the very least that these were not manufactured to consistent standards (see Section 5.4). Each of these factors may potentially influence toxicity. However, we will make the case that most of the observed severe harm is best understood in terms of these vaccines doing what they are designed to do; the harm is not accidental but rather built into the mRNA technology.

## 1.2 COVID-19 vaccines were never about your health

The official story of the COVID-19 "pandemic" is a staggering concoction of unscientific nonsense and outright lies [2]. This started already with the tales about the allegedly natural origin of the SARS-CoV-2 virus,

which became untenable as soon as Chinese virologist Li-Meng Yan and her colleagues published their detailed analysis of the viral genome, revealing unambiguous traces of laboratory manipulation [3, 4]. While we still don't know for certain who was or was not involved in the creation of this chimeric virus, this question is not really crucial: the absurd and predictably harmful "response measures", which were imposed swiftly and in lock-step by the WHO and by most national governments of the world, revealed clearly and early on that the virus and these measures were part of the same agenda. Already in early 2020, Klaus Schwab and Thierry Malleret, in their book *COVID-19: The Great Reset* [5], spelled it out for us:

> *The worldwide crisis triggered by the coronavirus pandemic ... is bringing economic disruption of monumental proportions. ... At the time of writing (June 2020), the pandemic continues to worsen globally. Many of us are pondering when things will return to normal. The short response is: never.*

The authors' patently false claim that the "pandemic continues to worsen" as of June 2020—see for example Figure 1.1—gives the game away: Klaus Schwab and his cronies at the World Economic Forum are using COVID-19 as a cudgel to inflict upon the world their premeditated "economic disruption of monumental proportions" and to usher in their dystopian "new normal." Early measures such as the closure of small businesses, schools, and places of worship caused grave damage to our livelihoods and our quality of life.

However, even worse was to come with the introduction of the gene-based COVID-19 vaccines. While there is now overwhelming evidence of grave injury and death due to these products (see Chapters 4 and 7), this evidence is still only slowly making its way into general awareness. A case can be made that these risks were not merely accepted but intended; the entire process of development and approval appears to have been designed to conceal the dangers and rush these harmful vaccines to market.

## 1.3 The misuse of emergency use authorizations, and the breakdown of regulatory safeguards

The first emergency use authorization (EUA) was granted in December 2020 by the FDA, and it concerned the Pfizer vaccine. Approvals of other vaccines, and by regulators in other jurisdictions, soon followed.

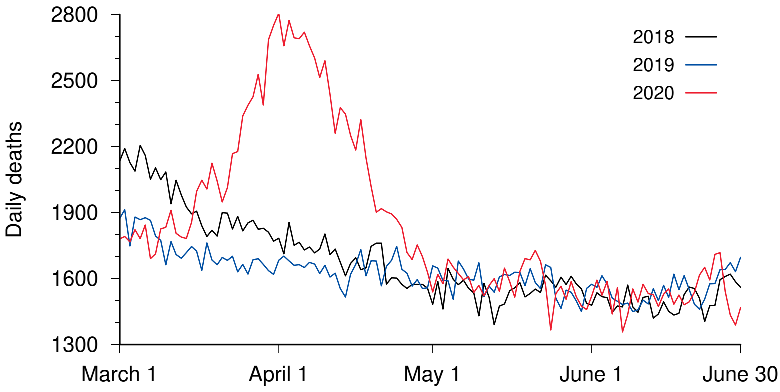



**Figure 1.1** All-cause mortality by day in France (including overseas territories) from March to June for the years 2018, 2019 and 2020. Figure adapted from a study by Rancourt et al. [6], who attribute the peak in March and April to the government's isolation measures that were imposed immediately after the WHO declaration of the COVID-19 "pandemic."

But were these hasty approvals really justified? The answer is no, for two reasons:

1. Already before the approvals, we knew that there was no real emergency. In mid to late 2020, several epidemiological studies had appeared which showed that the infection fatality rate of COVID-19 was on the order of 0.15% to 0.2% across all age groups, with a very strong bias towards elderly people who had comorbidities [7–9]. This rate does not exceed the range commonly observed with annually recurring waves of influenza, against which general vaccination is not considered necessary.
2. COVID-19 can be treated. Guidelines for such treatment were collaboratively developed by a large group of experienced physicians and published already in 2020 [10]. Treatment options are available both for the early stage of the disease, at which emphasis is placed on inhibiting viral replication, and for the later stage, at which anti-inflammatory treatment is most important [11]. Two drugs that have been used successfully at the early stage are hydroxychloroquine and ivermectin.

Ivermectin is also widely used in the treatment of tropical parasitic diseases such as onchocerciasis (river blindness), and for this reason it is on the WHO's list of essential medicines. Yet, with COVID-19, the

WHO saw fit to warn against the use of this very same well-known and safe drug outside of clinical trials [12]. Such a policy cannot be rationally justified, and it has quite appropriately been overridden by national or regional health authorities and ignored by individual physicians worldwide. With hydroxychloroquine, the situation is analogous.

The limited severity of the viral disease, and the availability of effective treatment void the rationale for the emergency use of vaccines against COVID-19; and this was already well understood when the first such authorizations were granted. But not only was there no valid rationale for even contemplating such EUAs—the issuance was based on incomplete and patently fraudulent documentation provided by the manufacturers. Some evidence of such fraud, which should have been caught by the regulators but apparently wasn't, is presented here in Section 2.9.

The cynical and reckless activity on the part of the manufacturers, the regulators and the health authorities has since continued. Pregnant women and breastfeeding mothers, who had been excluded from the abridged and perfunctory clinical trials, were nevertheless encouraged to receive the vaccines immediately after the EUAs had been given, which implies unacceptable risks for their fertility and for the health of infants (see Section 7.7). This risk is underscored by the detection of vaccine mRNA in the milk of breast-feeding mothers shortly after vaccination [13]. Moreover, even though reports of grave adverse events mounted rapidly in VAERS and other major databases, the EUAs have since been extended to ever younger age groups and now apply even to babies and infants.

The various contaminations detected in numerous production batches of the vaccines by third party investigators (see Section 5.4) reinforce the notion that nobody guards the vaccines' quality and manufacturing standards. It is clear, therefore, that the FDA and other national and international regulators no longer adhere to any traditional ethical and professional standards.

## 1.4 Why this book was written

While it remains necessary and urgent to inform the public of the risks and the manifest damage done by the COVID-19 vaccines, our main reason for writing this book was a different one. It is clear that the mRNA vaccine technology will soon be extended to pathogens other than SARS-CoV-2; as of this writing, clinical trials for such vaccines

against cytomegalovirus, Epstein-Barr virus, respiratory syncytial virus, an several others are already underway [14]. The purpose of this book is to show that we must expect these future mRNA vaccines to cause the same grave harm that is already manifest with those directed against COVID-19, and to do so in much the same manner. We want to help you understand that this harm is built right into the mRNA technology, and that you must do everything you can in order to protect your children and yourself from these future poisons dressed up as medicines.

# 2. Some elements of virology and immunology

The central thesis of this book is that the risks and the manifest harm which we have seen with the COVID-19 mRNA vaccines were predictable from first principles of immunology; and furthermore that similar harm must be expected with any future mRNA vaccines directed against other viruses or non-viral pathogens. In order to make this case, we will first briefly survey how viruses multiply, and how the immune system combats and ultimately overcomes viral infections. The discussion offered in this chapter will not be comprehensive; rather, it will present, in a simplified manner, only those elements which are crucial and indispensable for evaluating this book's thesis. For a more in-depth exposition, we must refer the reader to some of the appropriate standard works [15, 16].

## 2.1 The life cycle of a virus

You may be aware that viruses differ from other life forms by not being able to propagate independently, since virus particles are not cells; they merely consist of a nucleic acid genome (RNA or DNA), which is enwrapped by a shell consisting of proteins and oftentimes also lipids (fat-like molecules). Since they lack the cellular machinery for energy metabolism and for protein synthesis, they must use the cells of other organisms for their own propagation. To this end, the virus particles, or *virions*, must enter the cells of their host organisms and then direct those cells to manufacture offspring virions. This involves, at a minimum, the following steps (Figure 2.1):

1. A virion binds to a protein receptor on the surface of the host cell. This triggers the virion's uptake into the cell.
2. The virion undergoes *uncoating*. This releases the viral nucleic acid genome, which can now direct the synthesis of new copies of the viral proteins.

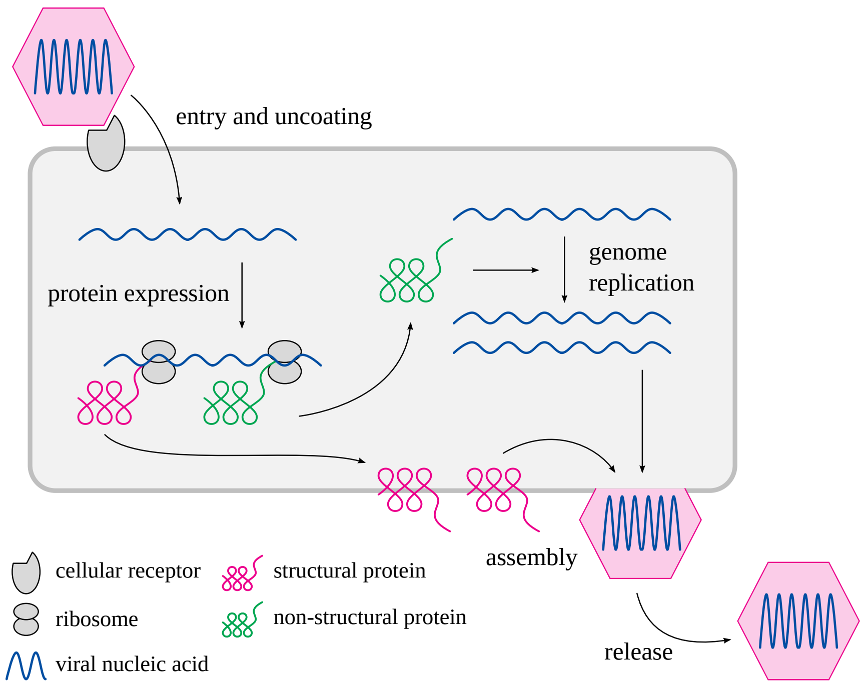



**Figure 2.1** Overview of viral multiplication and protein expression (simplified). A viral particle consists of a nucleic acid genome (DNA or RNA, blue) that is enclosed by viral proteins (magenta). These protect the nucleic acid and also mediate attachment to a host cell receptor, which facilitates entry into the host cell. Once inside the cell, the nucleic acid is uncoated and then directs the synthesis of new copies of the viral proteins. Non-structural viral proteins exist only at this intracellular stage and serve functions such as the replication of the viral nucleic acid. These new genome copies, together with the structural proteins, will assemble into new virions, which will be released from the cell and infect other cells in turn.

3. Some, but not all viral proteins will be incorporated into the daughter virions. Those which do not appear in the virions are referred to as *non-structural proteins*; they exist only within the infected cell and serve various purposes in viral multiplication, such as creating copies of the viral genome. Those proteins which *are* incorporated into viral particles are referred to as *structural proteins*.
4. New copies of the virus assemble at the cell surface, or sometimes within an intracellular compartment, and are then released from the cell. These progeny virions can then infect other body cells.

**2.1.1 Cellular vs. viral genome structure and protein expression.** Figure 2.1 was deliberately vague on the nature of the nucleic acid contained in the viral particles. There is in fact a great deal of variability—viral nucleic acids may be DNA or RNA, and they may be single-stranded or double stranded. The implications of this variability are quite interesting, but we won't discuss them here at length. Instead, we will just note that RNA viruses tend to have higher mutation rates than DNA viruses, and viruses with single-stranded genomes have higher mutation rates than those with double-stranded ones. Thus, single-stranded RNA viruses, including coronaviruses or polio virus, tend to have the highest mutation rates. This compounds the difficulties of vaccine development, because circulating viruses may evade vaccine-induced immunity by mutating to alter or lose some of the molecular features against which that immunity is directed.[1]

Figure 2.2 contrasts the mode of function of a cell's own genes to the genes of a coronavirus, which is shown here only as an example. The expression of cellular genes follows the regular pattern of transcription from the genomic DNA to messenger RNA (mRNA), followed by translation into protein. In contrast, coronaviruses contain a single-stranded RNA genome, which serves as the template both for protein expression and for its own replication. The replication involves a double-stranded RNA (dsRNA) intermediate, which exists only within the host cell but is never packaged into the viral particles. The RNA-dependent RNA polymerase that carries out these steps is encoded by one of the non-structural genes within the coronavirus genome.

As the figure suggests, dsRNA molecules have no role in cellular gene expression. Their presence inside a cell therefore indicates viral infection and ongoing virus replication. Remarkably, our body cells possess receptors which detect the presence of dsRNA and then acti-

[1]Whether or not a virus will be prone to such immunological escape will depend not only on its mutation rate but also on its degree of adaptation to the human host. For example, both influenza and measles viruses are single-stranded RNA viruses with high mutation rates, but of the two only influenza is prone to rapid "antigenic drift" by mutation, whereas the measles virus is virtually perfectly adapted to humans already, so that most mutations will offer it no selective advantage and therefore will not persist. SARS-CoV-2 seems to follow the influenza paradigm, however, as had to be expected from its recent manufacture in the laboratory, which did not allow for thorough evolutionary adaptation to the human host. (With influenza viruses, there is another source of genetic variation known as "antigenic shift." It is of major importance in principle, but not for the purpose of this book.)

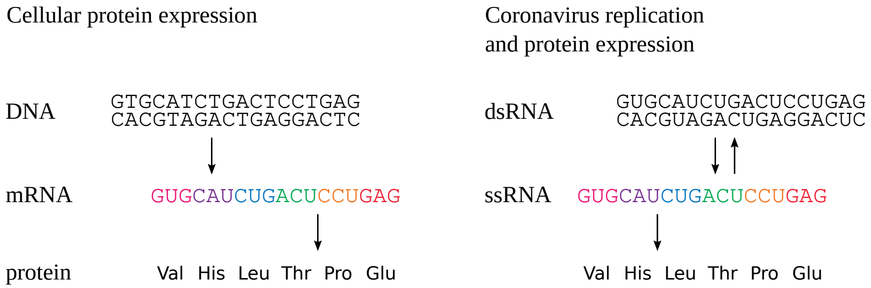



**Figure 2.2** The function of the coronavirus RNA genome, compared to cellular mRNA. Left: cellular genes are expressed by transcription of DNA to mRNA, which is then translated into protein. Right: the single-stranded RNA contained in coronavirus particles drives protein synthesis, too, but at the same time also serves as the template for its own replication, which involves a double-stranded RNA intermediate.

vate both non-specific and adaptive immune responses to the virus in question (see Section 2.2.2.1).

**2.1.2 The role of cellular receptor proteins in virus multiplication.** We just saw that the first step in viral entry and multiplication consists in binding of the virion to a cellular receptor protein. Of course, these cellular proteins do not exist for the purpose of facilitating viral entry; instead, they fulfill various roles in the physiology of the cell or the organism. For example, angiotensin-converting enzyme 2 (ACE2), a cellular protein which facilitates the entry of SARS-CoV-2, serves to degrade angiotensin II. This is a peptide (small protein) mediator that increases blood pressure. The binding of a virus to its receptor may interfere with that receptor's physiological function and thus cause some of the clinical manifestations of the infection; this is indeed the case with SARS-CoV-2 [11].

The requirement of the virus for specific cell surface molecules in order to infect those cells restricts the host cell range of most viruses. This limited host cell range tends to mitigate the severity of viral infections.

**2.1.3 Some viruses are surrounded by a membrane envelope.** In Figure 2.1, we drew the virus particle as consisting only of a nucleic acid and a protein shell (the *capsid*). While many viruses (e.g. poliovirus and adenoviruses) indeed contain only these two elements, others are additionally surrounded by an *envelope*, whose composition is similar

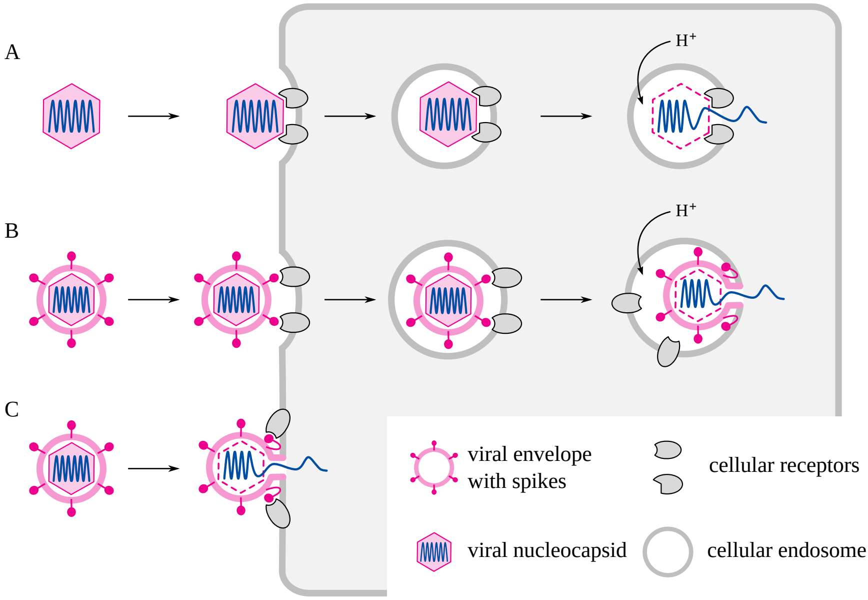



**Figure 2.3** Cellular entry and uncoating of non-enveloped and enveloped viruses. **A:** many non-enveloped viruses (e.g. adenoviruses) are taken up by endocytosis. Acidification of the endosome (i.e., the accumulation of $H^+$ ions within it) triggers uncoating of the viral genome and its transfer to the cytosol. **B:** many enveloped viruses (e.g. influenza virus) also follow the endosomal pathway. Transfer of the genome to the cytosol occurs when the viral envelope fuses with the endosome membrane. This step is triggered by a change in the molecular shape of the viral spike proteins, usually also driven by acidification. **C:** some enveloped viruses can fuse directly at the cell surface. Both of the pathways B and C have been suggested to occur with coronaviruses [15].

to that of a cell membrane, i.e. it consists of lipids and embedded membrane proteins. In this case, it is these membrane proteins which bind to the cellular receptors. They are often referred to as *spikes* or *spike proteins*.

In addition to engaging the cell's surface receptors, the spikes also mediate the fusion of the viral envelope to the cellular membrane, which can occur after endocytosis or directly at the cell surface. This fusion is an essential step in the transfer of the viral nucleic acid from the virus particle to the cytosol (the main compartment of the cell). Very commonly, this step is driven by the acidification of the *endosome*, i.e. the membrane compartment which after endocytosis contains the virus particle (see pathway B in Figure 2.3).

Coronaviruses are enveloped. The much talked-about spike protein of SARS-CoV-2, the virus which causes COVID-19, mediates both receptor binding and membrane fusion of this virus. In order to bring about membrane fusion, the spike protein must undergo a change in molecular shape ("conformation").

We note in passing that the well-known drugs chloroquine and hydroxychloroquine inhibit the acidification of endosomes. It is therefore not surprising that hydroxychloroquine is clinically effective against COVID-19 [17], as it is indeed with many other viral infections [15].

## 2.2 Immunity to viruses

Our immune system has a large arsenal of weapons, many of which are specifically tailored to bacteria, viruses, or other particular types of pathogens. Here, we will focus on those defense mechanisms which pertain to viral infections. These are also the most relevant ones for understanding the effects of mRNA vaccines—and not only antiviral vaccines such as those directed against COVID-19, but also possible future mRNA vaccines supposed to provide protection against tuberculosis, malaria or other non-viral infections.

We will start our exploration of antiviral immunity by posing two central questions:

1. What are the effector mechanisms which the immune system deploys in order to check and clear an ongoing virus infection?
2. The immune system learns from experience, such that in many cases we fall ill with the same virus only once and then remain immune to it for the rest of our lives. How does this learning take place?

**2.2.1 Antiviral immune effector mechanisms.** Our immune system combats virus infections using two key strategies:

1. it intercepts viral particles before they can infect our body cells, and
2. it destroys those body cells which have already been infected and are currently manufacturing progeny virions.

Both of these strategies involve molecules and cells which specifically recognize and bind the antigens (proteins) of the virus in question (Figure 2.4). The killing of infected cells is largely brought about by cytotoxic T-lymphocytes, also known as T-killer cells. Figure 2.4 illustrates how these are activated. The infected cell expresses viral proteins as instructed by the viral genome, but in the process it chops

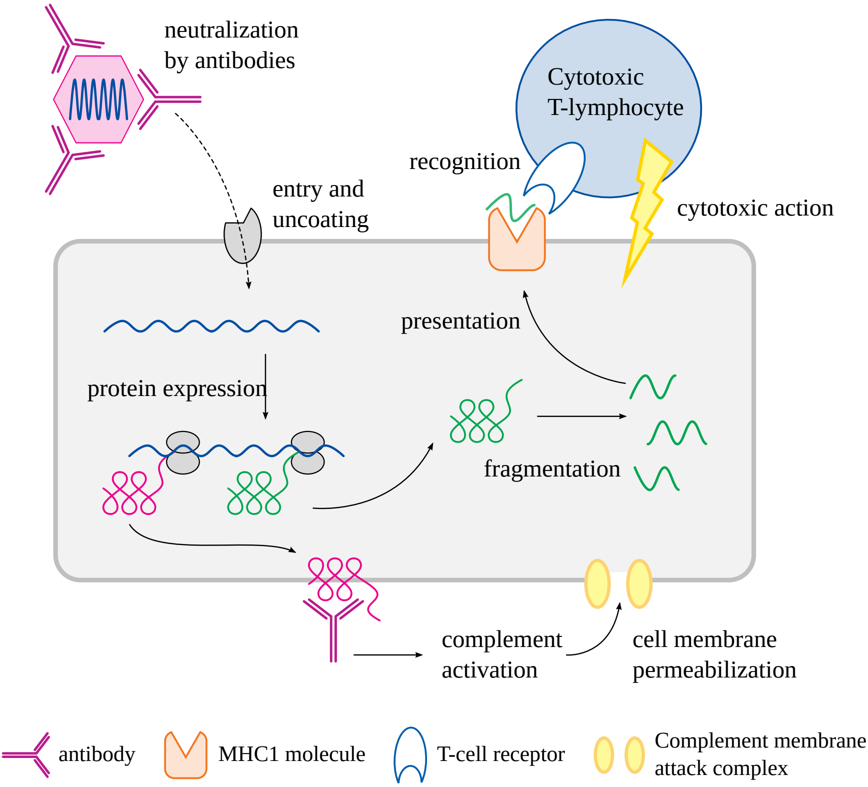



**Figure 2.4** Antiviral immune effector mechanisms. This cartoon illustrates three of the mechanisms by which our immune system combats and eradicates a virus infection. Antibodies can bind to viral particles and neutralize them, i.e. prevent them from binding to and entering our body cells. They can also bind to viral proteins that appear on the cell surface and then activate *complement*, a cascade of extracellular proteins that causes the formation of transmembrane pores in the virus-infected cells. Viral proteins which remain inside the cell can be fragmented and then exposed on the cell surface, bound to a special carrier protein (MHC1). Recognition of the MHC1-bound fragments by T-killer lymphocytes will activate these and cause them to unleash several cytotoxic proteins onto the virus-infected cell.

some of these protein molecules into small fragments. It then exposes these protein fragments (peptides) on the cell surface, bound to a specific carrier protein (MHC1). It does this at all times, whenever it synthesizes any proteins at all. This general mechanism is crucial to enable *immune surveillance*: the immune system can inspect those peptide fragments on the cell surface and determine whether the

cell is in good health or has been taken over by a virus and is now producing viral proteins. The surveillance is carried out by the cytotoxic T-lymphocytes. These cells possess specific surface proteins of their own, the *T-cell receptors*, which specifically recognize individual virus-derived peptides if these are presented by MHC1 molecules.

It is important to understand that there is a very large repertoire of T-cells with different T-cell receptors, out of which only one or a few, or possibly none at all, will bind to any given virus-derived peptide. A cytotoxic T-cell whose T-cell receptors do match and bind such a peptide will be thereby induced to attack the cell that presents it. The recognition event will also stimulate the cytotoxic T-cell to divide and multiply (more on this below).

Binding and interception of virus particles—*neutralization*—is mediated by antibodies, which are extracellular proteins synthesized and secreted by *plasma cells*. These cells are descended from B-lymphocytes, which also are induced to proliferate and maturate by encountering their cognate viral antigens (see Figure 2.7). As is the case with T-cells, there is a very large reservoir of B-cells with different surface receptors, out of which only a small subset will recognize any given antigen and then undergo activation.

Antibodies contribute to the killing of virus-infected cells in various ways. One such mechanism is also illustrated in Figure 2.4. It involves the *complement system*, which comprises a number of plasma proteins. The complement system is a self-amplifying cascade of proteases (protein-cleaving enzymes). It is activated by antibodies that have recognized and bound to their cognate antigens, which may be located on the surfaces of microbial cells or, with viral infections, on our own body cells. Complement activation culminates in the generation of a *membrane attack complex*, which is a large, ring-shaped structure, composed of multiple protein molecules, which quite simply punches a hole into the cell membrane.

Figure 2.5, which is taken from a seminal paper on the action mode of the complement system [18], illustrates that the complement system is perfectly capable of utterly destroying a cell. As you can see, the cells, which were exposed to antibodies and complement, are riddled with holes. The holes will break down the barrier function of the cell membrane, and the cell will die.

Membrane permeabilization is also one of the effector mechanisms deployed by cytotoxic T-cells. The pore-forming protein in question,

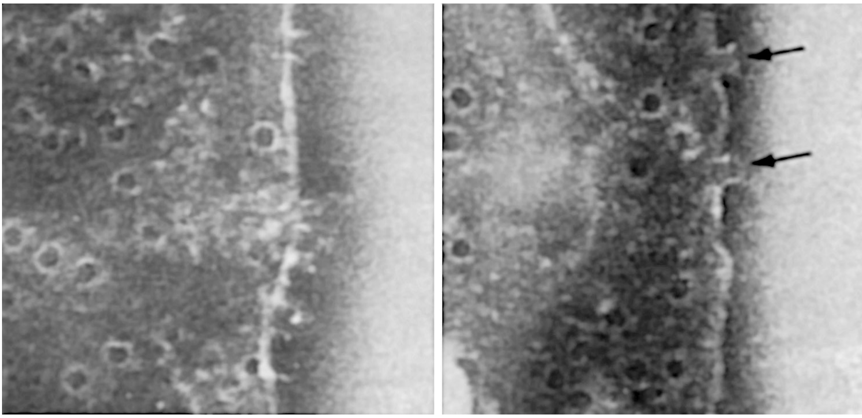


**Figure 2.5** Complement membrane attack complexes forming pores on red blood cells. Antibodies against sheep red blood cells were allowed to bind to such cells in the presence of human serum, which provided the complement proteins [19]. Most membrane attack complexes are viewed from the top. Arrows highlight individual complexes which sit on the edge of the cell; they are pictured sideways and can be seen to protrude from the cell surface.

*perforin*, is structurally similar to the main component of the complement pore (C9). This effect is augmented by the release of destructive enzymes from the T-cell, which can then enter the infected target cell through the perforin pores. In addition, the cytotoxic T-cells release mediators with induce the target cell to enter *apoptosis*—an innate program of cell suicide.

Antibodies and T-cell receptors share structural similarities, and as noted both are capable of specific antigen recognition. However, we should note the following differences between them:

1. antibodies recognize intact antigen molecules, whereas T-cell receptors recognize them only as fragments;
2. antibodies require only the antigen itself for binding, whereas T-cell receptors will recognize their cognate peptides (protein fragments) only when they are presented to them by MHC molecules.

Since antibodies are themselves extracellular proteins, they will encounter their antigens only if these are present either on cell surfaces or in the extracellular space. With such antigens, antibodies can be very effective. On the other hand, the fragmentation and MHC1-dependent presentation mechanism illustrated in Figure 2.4 enables the cytotoxic

T-cells to respond effectively to intracellular antigens. Thus, antibodies and cytotoxic T-cells clearly have complementary functions.

**2.2.2 The activation of an antiviral immune response.** We had noted above that both cytotoxic T-cells and B-cells are activated and induced to proliferate by contact with their cognate antigens, and that the T- and B-cells in question are drawn from a large preexisting pool of cells with different antigen specificities. While recognition of the specific antigen is indeed necessary for T- and B-cell activation, it is not the whole story: every specific immune response begins with the activation of innate, non-specific elements of our immune system.

**2.2.2.1 Specific immune responses are initiated by the non-specific immune system.** You likely know from experience that a contaminated wound can become inflamed—red, swollen, and painful—rather quickly. This swift reaction is not yet due to a specific immune response. Instead, the infecting microbes, which in this scenario are mostly bacteria, will initially activate our non-specific or innate immune system. This happens in two ways:

1. the microbial cells themselves will serve as triggers;
2. the toxic or invasive properties of the bacteria will kill some of our body cells. Some of the molecules released by decaying body cells will promote inflammation.

The complement system can be activated by bacterial cell surfaces even without the help of antibodies. Complement activation will not only permeabilize those bacterial cells, but also mark them for destruction by our *macrophages* and *neutrophil granulocytes*. These two cell types specialize in *phagocytosis*, that is, they professionally eat and kill microbes. A third phagocytic cell type are the *dendritic cells*. They are related to macrophages, but in contrast to the latter they function primarily as "messengers" rather than as "fighters"; they are crucial for triggering antibody responses to the pathogens they ingest and degrade (see Section 2.2.2.3).

Molecules released from killed bacterial cells—prominently cell wall components, but also bacterial DNA and others—will be recognized by various *pattern recognition receptors* (PRRs) within our own body cells. These PRRs are a large and structurally diverse group of proteins; a well-known subclass that you may have come across are the Toll-like receptors (TLRs). Activation of these various PRRs will induce the

release of many different inflammatory mediators, collectively known as *cytokines* and *chemokines*. Some important effects of these mediators are

1. increased vascular permeability. This floods the infected tissue with plasma proteins, including antibodies and complement;
2. attraction and activation of phagocytic cells and other immune cells toward the focus of infection; and
3. activation of the subsequent specific T-cell and B-cell response to the microbial antigens encountered at the site of the infection.

Viral infections activate their own appropriate PRRs. Some of these receptors respond to double-stranded **R**NA, which does not normally occur in human cells and therefore signals infection with an RNA virus.[2] Double-stranded **D**NA does of course occur in human cells, but not normally in the cytosol. Its presence in that cellular compartment therefore signals infection with a DNA virus; and accordingly it, too, is detected by a suitable PRR.

Yet other types of PRRs respond to molecules which are normally present only within healthy body cells but which may be released from decaying dead cells. In the context of microbial infection, such "hidden self" signals are useful for amplifying the immune response. On the other hand, they can also contribute to autoimmune disease: once autoimmunity has passed a threshold beyond which it can destroy our own body cells, the hidden self signals released by those destroyed cells will further incite and sustain the autoimmune aggression.

**2.2.2.2 Activation of cytotoxic T-cells.** Once the non-specific response to an infection has set the stage, the specific immune response will begin. We will now consider how the appropriate antigen-specific T-cell and B-cell clones are selectively activated, beginning with the cytotoxic T-cells.

We had seen that, whenever a cell produces a protein, a sample of those protein molecules will be chopped up into small fragments that are transported to the surface of the cell, where they become amenable to interaction with and recognition by cytotoxic T-cells. Envisage the

[2] Some PRRs will detect single-stranded RNA within endosomes, through which infecting viruses often gain entry (see Figure 2.3). Since mRNA vaccines are taken up via the endosomal route as well, they, too, may potentially activate these receptors. This effect can be suppressed by methyl-pseudouridine modification of the RNA [20], which is used by both the Moderna and the Pfizer COVID-19 vaccines (see Section 2.8.3.2).

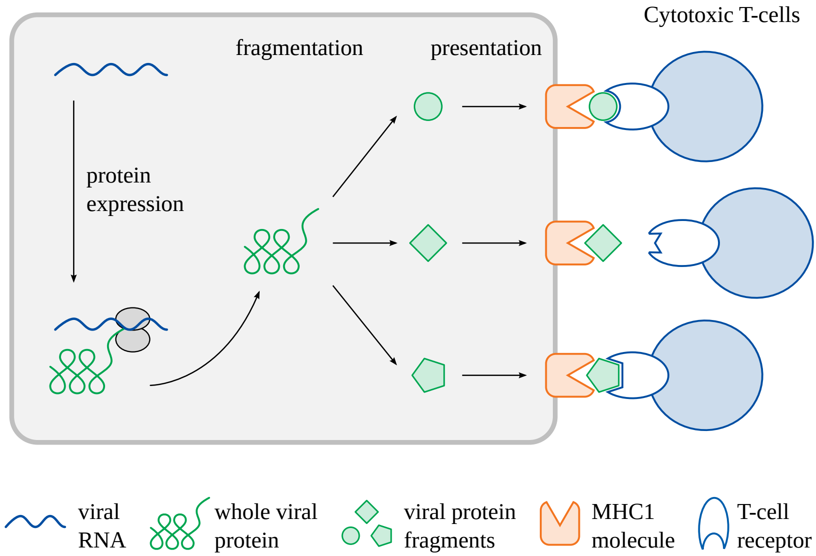



**Figure 2.6** Lock and key interaction of MHC1-bound protein fragments and T-cell receptors of cytotoxic T-cells. The T-cell receptors on our body's T-lymphocytes cover, collectively, a very large spectrum of antigen specificities, but all the receptor molecules on an individual T-cell are identical and bind to the same antigen. Only those T-cells which bind one of the protein fragments presented by a MHC1 molecule on a cell surface will be able to bind and be activated.

interaction between a cytotoxic T-cell and a presented protein fragment as one between lock and key (Figure 2.6). Our reservoir of cytotoxic T-cells contains myriad different locks (T-cell receptors), which can fit a virtually limitless variety of possible keys (fragments). Yet, the proteins of any given virus will only give rise to a limited number of keys, which will bind and activate only a correspondingly limited subset of all available cytotoxic T-cells.

It is imperative to note that any viral protein will give rise to many fragments, which will be recognized by many different cytotoxic T-cell clones—the number of activated T-cells is small only relative to the entire reservoir of available antigen specificities, yet it is still considerable in absolute terms. A new virus mutant may generate one or a few novel protein fragments, but the majority of other fragments will remain unchanged and therefore continue to be recognized by our T-lymphocytes. Analogously, some degree of cytotoxic T-cell-based cross-reactivity and cross-protection usually exists between different members of a

given virus family (see also Section 2.5). Thus, the narrative that the emergence of SARS-CoV-2 mutations must be countered, and that every "variant of concern" must be hunted down by the development of customized vaccines has been ridiculous from the start.

**2.2.2.3 Activation of antibody production.** As noted earlier, antibodies are extracellular proteins secreted by plasma cells, which are derived from B-lymphocytes, or B-cells for short. Like T-cells, the B-cells carry surface receptors whose antigen specificity will be very diverse among all B-cells, but will be the same for all receptors of a single B-cell. Unlike T-cell receptors, however, the B-cell receptors are actually antibodies. If a B-cell comes across a suitable antigen and binds to it via its receptor antibodies, then this B-cell will be activated: it will start dividing, and the daughter cells will eventually turn into plasma cells and start churning out soluble antibodies. The amount of antibodies produced collectively by the plasma cells in our bodies is rather large, even when no infection is present. Our blood plasma contains some 10-12 grams of antibodies per liter, and half of this amount will be replaced about every three weeks.

While with some B-cell subtypes the binding to antigen alone is sufficient for activation, most B-cells require additional stimulation by *T-helper* lymphocytes. The entire process is outlined in Figure 2.7. It begins with the uptake of the antigen in question by an *antigen-presenting cell* (APC), which can be a dendritic cell or a macrophage. Inside the APC, the antigen is fragmented and then presented on the cell surface. The process resembles the presentation of intracellular antigens on other body cells (see Figure 2.4); but note that antigen-presenting cells use a distinct type of MHC molecule. While the presentation of intracellular antigens to cytotoxic T-cells involves MHC class I molecules (MHC1), the presentation of originally extracellular antigens by specialized antigen-presenting cells involves class II molecules (MHC2). These MHC2 molecules interact selectively with T-helper cells rather than with cytotoxic T-cells.

A B-cell that has captured an antigen will recruit a T-helper cell by processing that antigen the same way an APCs does. Thus, the B-cell will generate the same complexes of MHC2 with antigen-derived peptides as an APC, which will enable it to interact with the same T-cell receptors. Once a T-helper has bound to a B-cell that presents a matching antigenic peptide, it will complete the activation of that B-cell.

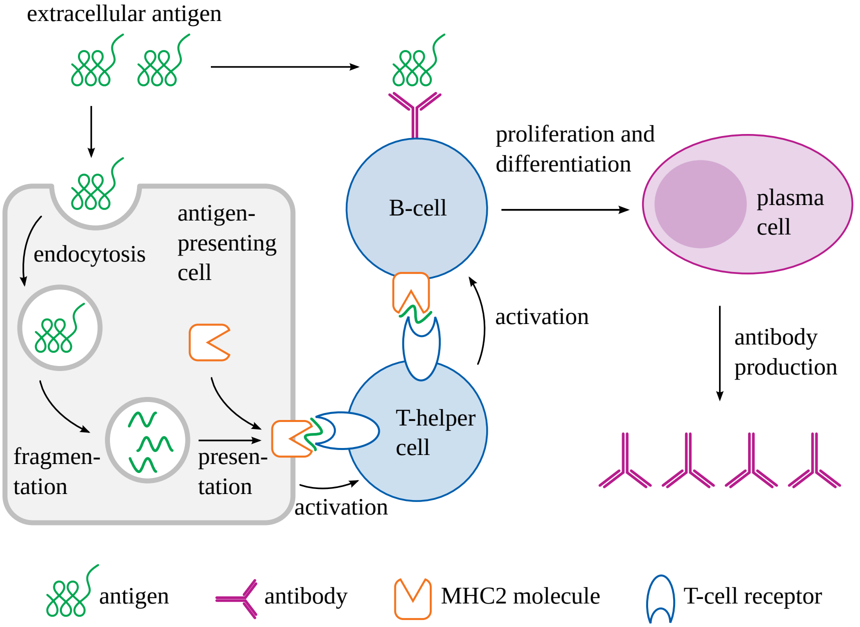



**Figure 2.7** Activation of antibody production. An extracellular antigen binds to an antibody on the surface of a B-cell, and also to an antigen-presenting cell (APC; usually a dentritic cell). Within the APC, the antigen is fragmented and then presented on the cell surface bound to a MHC class 2 molecule. This complex is recognized by a T-helper cell, which is thereby activated. The T-cell in turn activates the B-cell, which carries out the same antigen processing and presentation steps as the APC. In response to the dual activation by the intact antigen and the T-helper cell, the B-cell will start dividing. Its descendants will turn into plasma cells, which synthesize and secrete antibodies with the same antigen specificity as the original B-cell.

In summary, therefore, the activation of B-cells requires "permission" from both antigen-presenting cells and from T-helper cells; this somewhat complex arrangement serves to prevent premature and excessive antibody responses, particularly also against self antigens. These safeguards may yet fail, however, which may then result in autoimmune disease.

Looking back once more at Figure 2.4, we note that it shows antibodies binding to a viral protein which is located on the surface of a cell, but not extracellularly located. How might such a cell surface protein enter the MHC2 pathway of antigen presentation? This occurs downstream of cell destruction, for example after a cytotoxic T-cell

has killed the virus-infected cell in question. The remnants of that cell will then be dispersed and cleared away by macrophages and other antigen-presenting cells. Some of the remnants must also bind to the surface receptors of B-cells in order to activate the latter.

**2.2.2.4 The antibody class switch.** It is noteworthy that a newly formed plasma cell will initially produce a particular class of antibody called immunoglobulin M (IgM); after some weeks, it will switch over to another antibody class, most commonly IgG or IgA. The transient nature of IgM production is diagnostically useful: if an antibody response to a given antigen consists mostly of IgM, then it must be a primary response which began only recently; on the other hand, if it is mostly *not* IgM, then it has been going on for a while and may well be a secondary or "memory" response to an antigen that the immune system had already encountered previously (see Section 2.4).

Note that the class switch does not change the antigen specificity of the antibodies; thus, the IgG or IgA will continue to bind the same antigen as the initially formed IgM.[3]

## 2.3 How do the highly diverse T-cell and B-cell reservoirs originate?

Above, we likened the reservoir of T-cells and their receptors to a myriad of "locks", which between them will fit just about any antigenic "key"; and the same applies to our B-lymphocytes as well. It is now known that the truly incredible diversity of locks arises already during fetal development. How does this happen? Are locks molded in response to protein fragments (keys) as these appear during development? But then, the T-cells would be equipped with receptors exclusively recognizing "self" protein fragments, because the fetus in the womb is usually protected from infections, which means that no peptides derived from any infectious agents are available to train the developing T-cells. This could hardly serve a useful purpose. If, on the other hand, the diversity of locks should arise spontaneously and randomly, without requirement for any instructing key or template, then billions of lymphocytes might be generated that recognize "non-self" antigens, that is, those derived from extraneous agents including virus proteins.

Intriguingly, the latter is now known to be the case. However, the random nature of T-cell receptor generation also means that many

[3]While the antigen specificity of a maturing B-cell remains unchanged in principle, the binding affinity of its antibodies for their antigen *does* increase with time. This "affinity maturation" is driven by genetic point mutations.

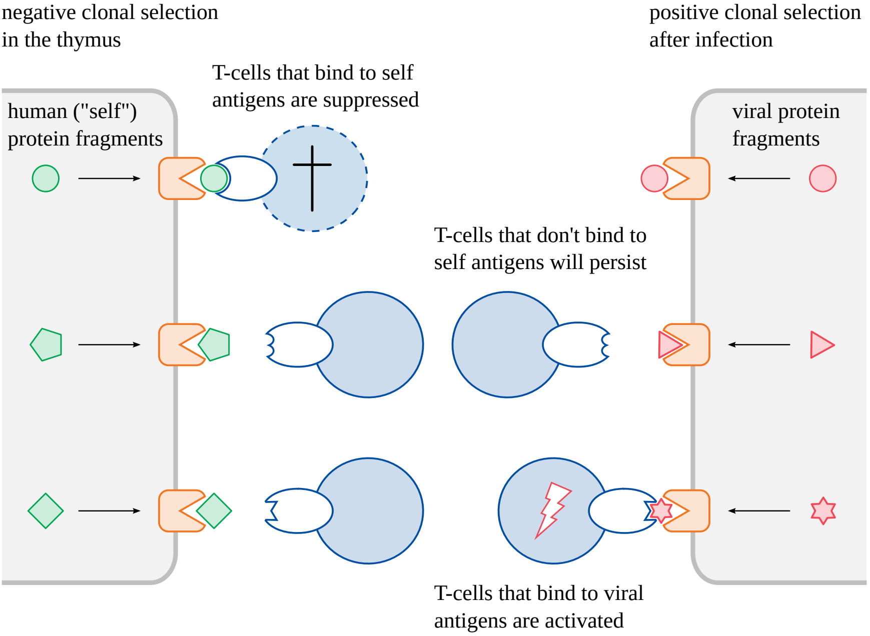



**Figure 2.8** Clonal selection of T-lymphocytes. The diversity of T-cell receptors is initially generated at random, which means that many T-cells will carry receptors that bind to self antigens. In the thymus, such T-cells are "baited" by cells that express those antigens and then destroyed or suppressed. Those T-cells which do not bind self antigens persist and may at a later time be activated and induced to multiply in response to a virus infection.

T-cells will recognize "self" antigens—those derived from proteins encoded by our own DNA. Wondrously, these lymphocytes recognizing "self" are silenced or held in check throughout life (Figure 2.8). Mishaps occasionally occur in this control mechanism that can lead to autoimmune disease. Come T-cells out of cover that are reactive against antigens expressed in liver cells—come autoimmune hepatitis. Come T-cells out of cover that are reactive against insulin-producing cells in the pancreas—come autoimmune diabetes.

But on the other hand, immune cells reactive against essentially all non-self proteins are present at birth and are ready to spring into action whenever a challenge is issued. It is for this very reason that conventional vaccinations can successfully be performed in early infancy, and also that even newborns are already able to withstand and overcome virus infections. Thus, when a Coronavirus comes around, up rises

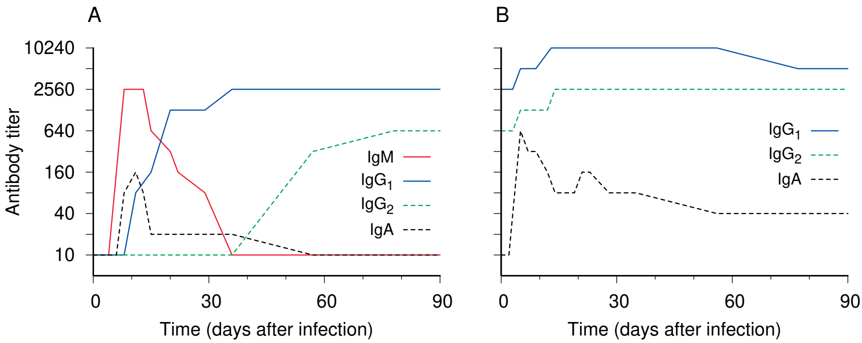



**Figure 2.9** Serum antibody responses to primary and secondary virus infection. In the experiment shown, a calf was infected twice with the same virus (bovine respiratory syncytial virus), and the concentrations of different classes of serum antibodies were measured over time. **A:** the first infection causes a transient rise of IgM antibodies, which is then supplanted by IgG. **B:** reinfection causes a rapid further rise in IgG, but IgM does not reappear. IgA rises transiently after the first infection but higher and more persistently after the second. Note the logarithmic $y$-axis. Adapted from Figure 1 in [21].

the anti-Corona team of T-cells; when flu comes around, up rises the anti-influenza team, etc. Each bout of training—each reinfection with the same, or more commonly a related viral strain—strengthens the team, enabling the virus to be more rapidly contained and the infection terminated with increasing effectiveness.

## 2.4 Immunological memory

An immune response to an acute infection is transient; once the infection is overcome, most of the inflammatory cells that were activated, including the T-cells, B-cells, and plasma cells discussed above, are no longer required and thus will be removed. This will also cause the level of circulating antibodies against the germ in question to decline with time. However, a certain number of T-cells and B-cells persist as so-called *memory cells*, often for life, and they can mount a rapid and robust secondary immune response upon renewed exposure to the same pathogen.

The difference between a primary antibody response and a secondary one is illustrated in Figure 2.9. The depicted experiment was carried out with a calf which had been raised without colostrum, i.e. it had not taken up any maternal antibodies. This was done to ensure

that any antibodies observed were produced by the calf's own, initially naive immune system.

The calf was deliberately infected with the same virus twice. The initial infection caused a somewhat delayed rise of antibodies. Initially, all of these antibodies were of the IgM class. IgM was then replaced with IgG antibodies, which remained persistently high on the time scale of this experiment, but after some more months would be expected to gradually decline also. A minor, transient IgA response was also apparent.

The second infection gave rise, after a shortened initial lag phase, to a further increase of IgG. Notably, IgM antibodies did not appear at all this time. The absence of IgM from the response to the second infection proves that no new B-cell clones were activated; instead, the antibody response was entirely driven by the multiplication of memory B-cells, which had already undergone the class switch from IgM to IgG or to IgA earlier.

Secondary T-cell responses, too, are more rapid and more forceful than primary ones. The clinical correlate of a secondary immune response is usually immunity—a renewed infection with the same virus will be contained before it becomes clinically manifest. The best examples of this are of course classical childhood diseases such as measles and rubella. Smallpox could once be considered a childhood disease as well, and it, too, used to leave behind lifelong immunity.

The increased effectiveness of secondary immune responses is of course the whole rationale of vaccination: the less effective primary response is elicited with an (ideally) harmless derivative of the pathogenic germ, so that the pathogen itself will meet with the secondary response even on first contact. While practically lifelong persistence of memory B- and T-cells has been reported after smallpox vaccination [22], vaccine-induced immunity may be less durable with other viruses, e.g. with measles and mumps [23, 24].

## 2.5 Cross-immunity

A very powerful feature of our adaptive immune system is *cross-immunity*: if we are infected by a virus which is new to us, yet related to a previously encountered one, then our immune system can recognize molecular features in the new virus that are familiar from the old one and mount a secondary response against these. At the same time, it will also mount a primary response against those features which are unique

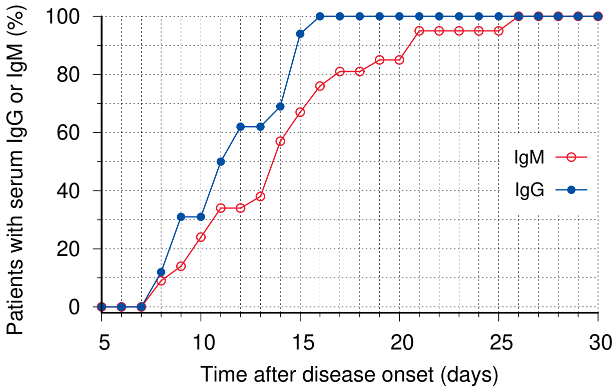



**Figure 2.10** SARS-CoV-2 antibodies in the serum of COVID-19 patients. IgG and IgM were separately measured in daily blood samples of COVID-19 patients. All patients eventually develop IgM antibodies as expected with a primary immune response, but IgG rises before IgM, indicating that the immune response is in part secondary in nature, which is due to cross-immunity. Data from Figure 1A and B in [25].

to the new virus and therefore novel. This explains findings such as those illustrated in Figure 2.10. The graph tracks the development of antibodies against SARS-CoV-2 in a group of COVID-19 patients who had initially tested negative for such antibodies. Both IgM and IgG rise up, but remarkably IgG rises faster. This rapid rise is typical of a response from memory. On the other hand, all individuals eventually develop IgM as well, which indicates that a primary response is taking place. Thus, the early rise of IgG results from cross-immunity, whereas the subsequent rise of IgM represents the primary response to the novel and unique antigenic features of SARS-CoV-2.

The specific viruses most likely to have laid the groundwork for the memory-type reaction to SARS-CoV-2 infection are evident from the data in Figure 2.11. In this study, serum samples from COVID-19 patients were tested for antibodies that would cross-react with the spike proteins of four other human coronaviruses, namely, SARS-CoV-1, MERS, HKU1, and OC43. In each case, SARS-CoV-2 infection significantly increased antibody levels relative to those observed in a control group of individuals not infected with SARS-CoV-2. What is more, however, with the endemic virus strains HKU1 and OC43, even the negative control group displayed fairly high antibody levels, which indicates widespread previous infection with and immunity to these

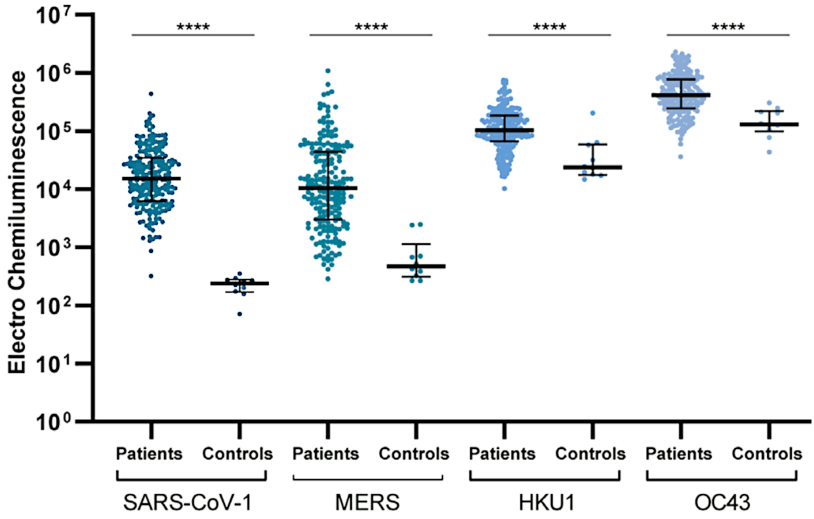



**Figure 2.11** Cross-reactive IgG antibodies induced by SARS-CoV-2 infection. Serum samples from 203 individuals with evidence of SARS-CoV-2 infection and from a negative control group were assayed for the levels antibodies to the spike proteins of human coronaviruses SARS-CoV-1, MERS, HKU1, and OC43. With all four antigens, antibody titers were higher in infected patients than in controls, indicating that antibodies to the SARS-CoV-2 spike cross-react with those of the other coronaviruses. Figure adapted from [26].

strains. If someone with such immunity is infected with SARS-CoV-2, then cross-reactive memory B-cells induced earlier by HKU1 or OC43 will be reactivated to again produce antibody. It is noteworthy that the presence of such cross-reactive antibodies correlates with reduced clinical severity of COVID-19 [27].

With SARS-CoV-1 (the original SARS virus) and with MERS, which never were endemic in the human population, antibody levels were low among the control group. In these cases, the strong increase in the level of cross-reactive antibodies among COVID-19 patients must have been induced by SARS-CoV-2 itself. We can therefore expect that recovered COVID-19 patients would enjoy a measure of cross-protection from SARS or MERS, should either virus stage a comeback, for example by eloping from another "high-security" bioweapons laboratory.

Cross-immunity between SARS-CoV-2 and other coronaviruses has also been documented with respect to T-lymphocytes [28, 29]. Most likely, widespread preexisting T-cell and B-cell cross-immunity accounts for the rather benign clinical course of COVID-19 in most patients.

## 2.6 Who really controls viral infections: antibodies, or cytotoxic T-cells?

We have seen that virus infections elicit both antibody formation and a T-cell response. What is the respective importance of each in controlling and overcoming the virus infection? The answer is: it depends.

**2.6.1 Primary vs. secondary immune response.** In the first infection with a given virus (and in the absence of cross-immunity), there are no antibodies which could bind and neutralize the virus particles before entering our body cells. Therefore, by the time an immune response has been mounted, a considerable number of cells may have been infected, which then have to be eliminated. This task falls primarily to the cytotoxic T-cells, although antibody-dependent cytotoxic mechanisms also contribute (see Figure 2.4). On the other hand, if we had encountered the infecting virus before, and antibody levels are still sufficient or can be raised on short notice, then these antibodies can effectively limit the spread of the virus and therefore have a dominant role [16, p. 358].

**2.6.2 Antibody-dependent enhancement.** The answer also depends on the identity of the virus. While all viruses will induce specific antibodies, some viruses will not be effectively neutralized by them. This can occur because certain cells of the immune system are supposed to take up antibody-antigen complexes and destroy them. If a virus particle to which antibodies have bound is taken up by such a cell, but manages to evade destruction, then it may instead start to multiply within that immune cell. Overall, instead of protecting our cells from the virus, the antibodies will then promote the replication of the virus and worsen the disease. This effect is called *antibody-dependent enhancement* (ADE). Clinically, ADE can cause a hyperinflammatory response (a "cytokine storm") that will amplify the damage to our lungs, liver and other organs of our body.

Dengue fever is a natural virus infection that is often complicated by antibody-dependent enhancement; this will cause recurrent infections to be more severe than primary ones. ADE has also been observed after vaccination against dengue virus, respiratory syncytial virus (RSV), and measles. Coronaviruses, too, are prone to vaccine-elicited ADE; it has been described with the original SARS virus (SARS-CoV-1), the MERS virus, and feline coronavirus [30, 31]. All of these are closely related to SARS-CoV-2. SARS-CoV-1 in particular is highly homologous with SARS-

CoV-2, with 82% sequence identity at the genome level, and the viral receptor on host cells for both is ACE2. The risk of antibody-dependent enhancement in connection with COVID-19 infection and vaccination was explicitly recognized in the literature before the gene-based COVID-19 vaccines were rolled out [32–35], yet it was not rigorously evaluated during the very short clinical trials.

**2.6.3 Viral evasion of T-cell cytotoxicity.** While ADE permits some viruses to evade antibody-mediated neutralization, other viruses prevent the activation of cytotoxic T-cells by interfering with the MHC1-dependent antigen processing and presentation pathway outlined in Figure 2.4. Well-known examples are members of the Herpesvirus and the Poxvirus families [36].

Our immune system has an answer—the *natural killer* (NK) cells. These are lymphocytes with a peculiar set of surface receptors that can detect the *lack* of MHC1 molecules on other cells in our body, which indicates that the MHC1-dependent pathway is being tampered with in those cells. The NK cell will thereby be activated to kill those cells. NK cells can also be activated by antibodies bound to viral proteins on the surface of infected cells.[4]

In summary, cytotoxic T-cells will be most important in primary infections and with those viruses that induce ADE, whereas antibodies will have a dominant role in secondary infections and with those viruses that can evade the action of cytotoxic T-cells.

## 2.7 Immunity to respiratory viruses: systemic versus mucosal immunity

Many vaccines, including the COVID-19 ones, are aimed at viruses that infect primarily the mucous membranes of the respiratory tract before possibly spreading through the bloodstream to other organs of the body. In this context, we must note that the cells of the immune system which reside within and beneath the mucous membranes of the respiratory tract (and also of the digestive and genitourinary tracts) function somewhat independently from those immune cells which protect the interior of the body.

[4] The combined effect of antibodies and NK cells is referred to as 'antibody-dependent, cell-mediated cytotoxicity' (ADCC). Furthermore, NK cells are also endowed with pattern-recognition receptors for viral nucleic acids and some viral proteins. This permits them to combat a viral infection even before a full-fledged adaptive immune response sets in—they participate in both innate and adaptive immune responses.

One key feature of the functional distinction between mucosal and systemic immunity are the two major categories of antibodies which are present in the body. Antibodies in the first category are produced by plasma cells which are located within a mucous membrane, directly beneath its uppermost cell layer (the *epithelium*). These antibodies—secretory immunoglobulin A (sIgA)—are secreted to the surface of the mucous membrane. They are thus on site to meet air-borne (or food-borne) viruses, and they may be able to prevent viral binding and infection of the cells within the mucous membrane.

The antibodies in the second category—IgG and circulating IgA—occur in the bloodstream. These antibodies can potentially counteract the spread of viruses via the bloodstream, for example when mucosal immunity fails to repel an infection of the airways or to confine it to the cells of the mucous membranes alone.

Crucially, vaccines that are injected into the muscle—i.e., the interior of the body—will only induce IgG and circulating IgA, *but not secretory IgA*. The antibodies induced by such vaccines therefore cannot and will not effectively protect cells of the respiratory tract against infection by air-borne viruses [37, 38]. This realization is neither contentious nor particularly new. Even 30 years ago, McGhee et al. [38] concluded:

> *It is surprising that despite our current level of understanding of the common mucosal immune system, almost all current vaccines are given to humans by the parenteral route [i.e. by injection]. Systemic immunization is essentially ineffective for induction of mucosal immune responses. Since the majority of infectious microorganisms are encountered through mucosal surface areas, it is logical to consider the induction of protective antibodies and T cell responses in mucosal tissues.*

The failure of intramuscular injection to induce secretory IgA was confirmed yet again in a recent study on Middle East Respiratory Syndrome (MERS) [39], which like COVID-19 is caused by a coronavirus of dubious origin. The experimental vaccine used in this study was gene-based, like the major vaccines currently deployed against COVID-19. With Pfizer's COVID-19 vaccine, only feeble and short-lived induction of mucosal antibodies has been detected [40, 41]. With little or no secretory IgA, there is no reason to expect that vaccination will effectively inhibit replication of the virus within the mucous membranes. One therefore had to expect the failure, meanwhile manifest [42, 43],

of the vaccines to prevent upper respiratory tract infection with the SARS-CoV-2 coronavirus, and thereby the spread of the virus.

The only thing that will effectively induce secretory IgA antibodies (sIgA) are naturally occurring airway infections, or possibly intranasally applied vaccines, which however so far are experimental [39].[5] The mucous membranes of healthy individuals are consequently coated with antibodies directed against common respiratory viruses. However, the capacity of these antibodies to prevent infections is limited, which is why infections with air-borne viruses occur repeatedly throughout life.

The subordinate role of secretory IgA in combating systemic viral infections is highlighted by the fact that individuals with a very common genetic defect (selective sIgA deficiency) who are unable to produce sIgA do not suffer from dramatically increased susceptibility toward severe respiratory infections. Severe infections that spread beyond the respiratory mucous membranes will encounter the systemic part of the immune system, which protects the interior of the body, and which remains intact in patients with the above gene defect. This part includes the antibodies found in the bloodstream, i.e. IgG and circulating IgA.

## 2.8 Vaccination strategies

We will now consider the different types of antiviral vaccines, beginning with the conventional ones. While these are not the focus of this book, discussing them briefly will give us some useful background for evaluating the mRNA vaccines.

Among the conventional antiviral vaccines, a key distinction is that between infectious or "live" virus vaccines on one hand, and non-infectious or "dead" ones on the other. Both types are widely used and have their respective strengths and weaknesses.

**2.8.1 "Dead" vaccines.** These vaccines consist of virus-derived antigens that are incapable of replicating. The traditional method for preparing such vaccines consists in chemical inactivation—the virus in question is grown in eggs or in a suitable cell culture and then treated with some chemical which will react with the viral particles and thereby

[5] One vaccine that *was* delivered in a biologically appropriate manner was the Sabin live vaccine against polio: it was given orally, which mimics the route of infection with the natural poliovirus. However, do to serious safety concerns (see below), this vaccine is now obsolete.

destroy their ability to infect cells and replicate. A suitable procedure is described in a recent report on the development of an inactivated COVID-19 vaccine [44]. The vaccine now marketed by the Chinese company Sinovac is of this kind. Another important example is the Salk vaccine against poliomyelitis, which has reclaimed its leading place from the Sabin live polio vaccine due to the severe safety deficits of the latter (see Section 2.8.2.3).

A potential risk of traditional dead vaccines is that some infectious particles might survive the chemical inactivation process. This risk is absent with *subunit vaccines*, which have become feasible with the advent of recombinant DNA technology. A good example is the hepatitis B vaccine. Its only antigenic component is the surface antigen of the virus particle, which is recombinantly expressed in vitro; no intact viral genome, and therefore no infectious particles, are present at any stage of the production process.

While both chemical inactivation and recombinant subunit expression may reduce or even abolish not only the infectiousness of a virus but also the toxic activities of its viral proteins, the latter is not a given. We note specifically that the "Novavax" subunit vaccine, which contains the SARS-CoV-2 spike protein as the only antigen, has been linked to cases of myocarditis [45], as have of course the gene-based COVID-19 vaccines [46, 47].

How does the immune system respond to these dead vaccines? It will process them as extracellular antigens, that is, they will be taken up and processed by antigen-presenting cells and then induce the activation of cognate T-helper and B-cells, leading to antibody production (see Section 2.2.2.3). In contrast, no or very little activation of cytotoxic T-cells will take place. Moreover, since these vaccines are injected subcutaneously or intramuscularly, induction of mucosal immunity will be weak or absent.[6]

**2.8.2 Live virus vaccines.** These vaccines are actual viruses that are either *attenuated* versions of the pathogenic virus in question, or they

[6]Partial protection from infection by mucosal immunity has been reported for example with an inactivated polio vaccine [48]. Some degree of cytotoxic T-cell activation is possible through *cross-presentation*, i.e. through "spillover" of antigens from the MHC2 pathway into the MHC1 pathway of antigen presentation and T-cell activation [49, 50]. It should be noted, however, that with polio the main goal is not to inhibit mucosal infection but rather the spread of the infection through the bloodstream to the central nervous system (see Section 2.8.4). This is indeed readily achieved by the Salk vaccine.

are natural viruses distinct from the pathogen but related to it. The latter case is best illustrated by Edward Jenner's invention of using the natural cowpox virus for vaccinating against smallpox. This procedure is also an excellent illustration of cross-immunity (see Section 2.5). The Vaccinia virus strains which were used for smallpox vaccination in the twentieth century are derived from other natural poxviruses of somewhat unclear origin [51].

In contrast, the Sabin polio vaccine and the measles vaccine are live vaccines that were derived in the laboratory through serial passage in non-human cell cultures. The principle of attenuation is simply to "encourage" the virus to adapt to its non-human host cell environment. At least some of the spontaneous mutations that help the virus grow better in non-human cells will reduce its ability to propagate in human hosts. Thus, if the virus is introduced into humans afterwards, it will tend to cause only mild infections, which however will still suffice to induce a protective immune response.

Since live virus vaccines are actual viruses, they tend to induce both antibody and cytotoxic T-cell responses; that is, the immune response more closely resembles that to the original pathogen, and therefore it can be expected to be more robust and enduring. While this consideration favors live over dead vaccines, the live vaccines nevertheless have their own specific drawbacks.

**2.8.2.1 Atypically severe infection in susceptible individuals.** The virulence of the vaccine virus may be sufficiently low for healthy recipients, but those with predisposing conditions, such as immune disorders or skin diseases, may suffer severe disease after inoculation. For example, smallpox vaccination is contraindicated in persons with atopic eczema (neurodermatitis), since in them the vaccine virus may cause a systemic skin disease known as *eczema vaccinatum* [52]. Even in recipients without recognizable predisposition, smallpox vaccination has caused myocarditis and encephalitis, i.e. infection of the heart and the brain, with often severe and sometimes fatal consequences.

**2.8.2.2 Transmission of the vaccine virus in the human population.** Since the vaccine is a live virus, it may spread from vaccinated individuals to bystanders, and possibly onward from the latter throughout the human population. While superficial examination might suggest such transmission to be a good way for increasing the effectiveness of live vaccines [53, 54], it poses unacceptable risks, for the following

reasons: the vaccine might be transmitted to persons who are at risk of severe disease from it (see above), and the virus might even revert to full virulence while spreading in the human population. Unfortunately, the latter risk is not merely hypothetical.

**2.8.2.3 Reversion of the attenuated virus strain to full virulence for humans.** We noted above that the process of attenuation relies on the serial passage of the virus in non-human cells, which will select random mutations that enhance growth in these cell cultures, but at the same time decrease virulence for humans. Conversely, if such an attenuated virus is inoculated into humans, then this will initiate a serial passage in human cells, which will select for mutations that revert or compensate the attenuating ones. This effect will be magnified if the virus can be transmitted from vaccinated to non-vaccinated individuals.

The occurrence of such vaccine-derived revertants is well documented with oral poliomyelitis vaccines, and some of these revertants have caused large outbreaks in the human population. A detailed study on a cluster of such outbreaks, which had occurred in Nigeria, documented 403 cases of paralytic disease and an estimated 700,000 total infections. Furthermore, the study suggested that revertant virus strains emerged multiple times during these outbreaks [55]. This example should suffice to illustrate the seriousness of the problem, which is the reason that the world has switched back to the safer dead polio vaccine.

**2.8.3 Gene-based vaccines.** You are likely aware that two different types of gene-based vaccines are being used against COVID-19, namely, the adenovirus-based ones produced by AstraZeneca and Johnson & Johnson, and the mRNA vaccines produced by Pfizer and Moderna. We will limit the discussion to these two types, even though there are other experimental variations on the theme.

**2.8.3.1 Adenovirus-based vaccines.** Adenovirus particles contain double-stranded DNA genomes, which they release within their host cells. An infected cell first transcribes the viral genome to mRNA, from which it then translates the viral proteins (see Figure 2.12). In adenovirus-based vaccines, several genes of the natural adenovirus genome have been replaced with the gene encoding the vaccine antigen in question. In case of the adenovirus-based COVID-19 vaccines, this is the gene encoding the SARS-CoV-2 spike protein.

It is noteworthy that a cell infected with such a recombinant adenovirus particle will produce both the SARS-CoV-2 spike protein and those proteins of the adenovirus carrier ("vector") whose genes remain part of the recombinant genome. Accordingly, an immune response will be elicited against all of these proteins. Some of the antibodies raised against the adenoviral proteins after the first injection can neutralize the recombinant virus particles, and they will therefore reduce the effectiveness of booster injections.

We further note that the deletion of some of the naturally occurring adenovirus genes from the recombinant genome leaves this vaccine virus "crippled"—it is able to infect human cells and to induce protein synthesis within them, but it is unable to replicate and to generate any progeny virions. This means that the entire amount of virus particles required to stimulate an immune response must be injected at once, instead of building gradually in vivo as would be the case with a natural virus infection or a conventional live virus vaccine. The injection of such a large dose of viral material may aggravate adverse events.

**2.8.3.2 mRNA vaccines.** An mRNA vaccine particle contains a synthetic mRNA, which is encased in a shell composed of various types of lipids, a *lipid nanoparticle* (LNP). These lipids protect the RNA in the extracellular space, and they also facilitate its uptake into the host cell. This uptake is essentially not restricted by cell type—any cell can take up these mRNA/lipid nanoparticles, even though the cells of certain organs—e.g., liver, spleen, and ovaries—accumulate particularly high amounts, for reasons that will be explained in Section 5.2.1.

Once inside the cell, the synthetic mRNA sheds its lipid shell and then functions like a natural mRNA to induce the synthesis of the protein it encodes. With the COVID-19 mRNA vaccines, this is again the SARS-CoV-2 spike protein. Note, however, that with both the Pfizer and the Moderna COVID-19 vaccines, the synthetic mRNA carries a peculiar modification: one of the four nucleosides contained in natural mRNA, namely uridine, has been artificially replaced with 1-methylpseudouridine.[7] This causes a very substantial increase in the level of

[7]The mRNAs in the Pfizer and the Moderna vaccines carry two additional modifications: their nucleotide sequences are *codon-optimized* for maximal expression in human cells, and they carry two strategic point mutations which stabilize the spike protein's *pre-fusion conformation*, i.e. they inhibit the change in the molecular shape of the spike protein that normally accompanies the fusion of the viral envelope with the cellular membrane (see Figure 2.3).

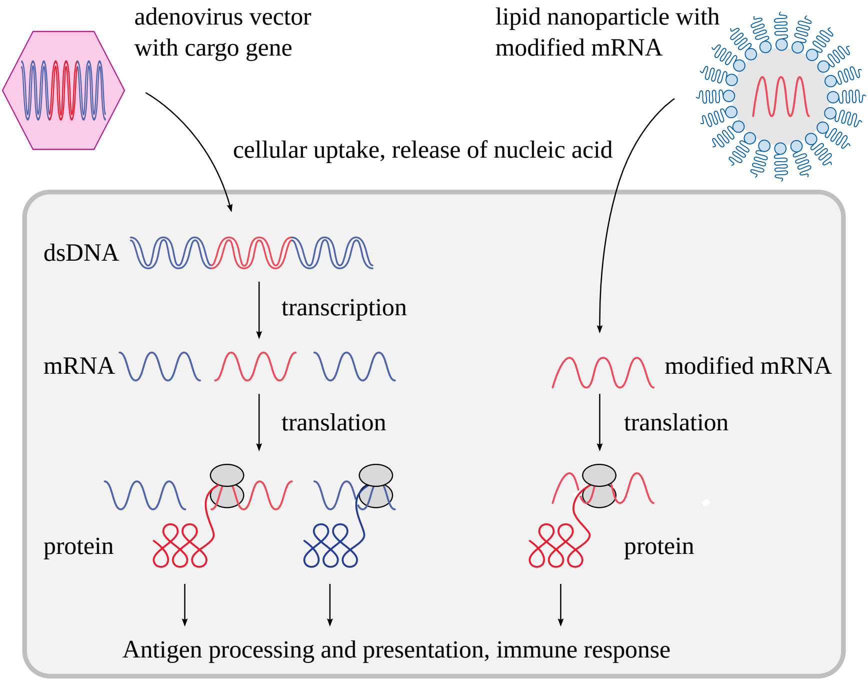



**Figure 2.12** Action mechanisms of gene-based vaccines. Left: adenovirus-based vaccines contain a cargo gene (red) within their recombinant double-stranded DNA genome, which is expressed within the cell much like a cellular gene. Right: mRNA vaccines consist of a modified mRNA that is encased in a shell of lipids, which facilitate the uptake of the mRNA into host cells. It is then directly translated into antigenic proteins. Antigen processing and presentation proceed as illustrated in Figures 2.4 and 2.7.

translation—much more spike protein will be produced than would be the case with a natural uridine-containing mRNA [56, 57].

The synthetic mRNA encodes no other protein than spike—in contrast to the adenovirus-based vaccines, no other viral proteins are involved in the function of mRNA vaccines. Since the mRNA does not replicate inside the host cell,[8] the full amount of nucleic acid required to produce the necessary quantity of protein antigen must again be injected at once.

[8]This applies, at least officially, to the COVID-19 vaccines supplied to the public. However, Pfizer has developed and conducted clinical test with self-amplifying mRNA vaccines, which do encode additional viral genes. Such vaccines have not yet been deployed outside limited clinical trials.

**2.8.3.3 The immune response induced by gene-based vaccines.** Both forms of gene-based vaccines induce the intracellular production of antigenic protein; therefore, they should in principle lend themselves to the MHC1-mediated induction of a robust cytotoxic T-cell response (see Figure 2.4). However, since the spike protein encoded by all gene-based COVID-19 vaccines is transported to the cell surface, it will end up mostly in the MHC2 pathway of antigen presentation. One would therefore expect a preferential activation of T-helper cells and a strong antibody response, but a rather feeble induction of cytotoxic T-cells. According to the limited evidence available, this is indeed the case [58].[9]

While the gene-based vaccines may superficially resemble natural viruses or live virus vaccines, the devil is in the details—the apparently minor differences in the action modes have profound implications for the likelihood and distribution of adverse events. This will be discussed in Section 3.3.

**2.8.4 Degrees of vaccine-induced immunity, and rationales for vaccination.** The ideal outcome of vaccination would be *sterilizing immunity*, that is, the virus in question will no longer be able to infect the recipients of the vaccine. The vaccinees will thereby not only be protected from clinical disease, but will also deny the virus any opportunity to propagate. If a high enough proportion of the population has received such a vaccine, then the result should be *herd immunity*: the likelihood of each case of the infection to spawn another case—the *basic reproductive number*—will drop below 1, which means that the infection will peter out rather than tear through the entire population. In theory, herd immunity is also possible with a vaccine which merely reduces but does not entirely abolish infection in vaccinated people; however, it is difficult to come up with compelling real-world examples.

A vaccine that does not suppress infection may still protect from significant clinical disease. For example, poliovirus initially infects the mucous membranes of the gut, and it is from there that the virus is shed and propagated. However, this intestinal infection amounts to no more than an episode of diarrhea. The characteristic paralytic disease occurs only if the virus spreads from this initial site of propagation

[9] For an apparent example to the contrary, see Section 4.4.6, which discusses a clinical case in which cytotoxic T-lymphocytes against spike, but not spike protein itself, were detected within the liver.

first into the bloodstream and then to the central nervous system. As noted in Section 2.7, intramuscularly administered vaccines will not effectively induce mucosal immunity, and indeed poliovirus can still propagate in many of the vaccine recipients [48]. However, the intramuscularly injected dead polio vaccine *will* effectively induce antibodies that circulate in the bloodstream, and these will reliably neutralize the virus before it can infect the central nervous system and induce paralytic disease.

A vaccine that does not prevent severe disease might nevertheless mitigate it; however, again it is difficult to find realistic examples, at least from the sphere of viruses. With respect to bacterial diseases, a valid example may be the original tuberculosis vaccine, which is an attenuated live vaccine.

An intriguing benefit of herd immunity is that it protects not only the vaccine recipients, but also the non-recipients, including those in whom vaccination is inadvisable, because they are predisposed to adverse reactions to the vaccine. However, it is self-evident that only when herd immunity is actually feasible can a case be made to impose mandatory vaccination on the healthy majority for the sake of protecting the vulnerable few. The COVID-19 vaccines, which were foisted on the public with ruthless coercion, have never come close to meeting this requirement.

## 2.9 Appendix: some evidence of fraud in Pfizer's clinical trials

Having covered some fundamentals of the antiviral immune response, we are now ready to critically assess some of the clinical trial data that Pfizer submitted to the regulators when applying for emergency use authorization. A key illustration that occurs in the reports by both the FDA [59] and by the EMA [60] compares the cumulative incidence of COVID-19 among the vaccinated and the placebo group. This graph, which is shown as Figure 9 in the EMA report, is here shown in Figure 2.13A. Up to day 12 after the first injection, the cumulative incidences in the two groups track each other closely. After day 12, however, only the placebo group continues to accumulate further new cases at a steady pace, whereas the slope of the graph abruptly drops to almost zero in the vaccine group.

This remarkable observation suggests that immunity set in very suddenly and uniformly on day 12 exactly among the vaccinated. Since the second injection occurred 19 or more days after the first one, this

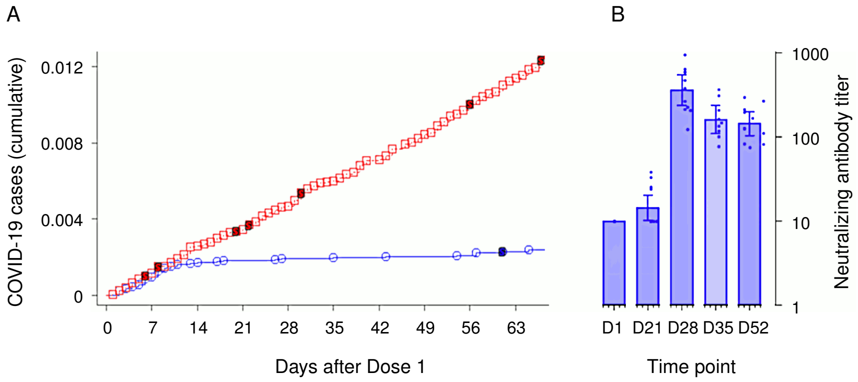



**Figure 2.13** Evidence of fraud in Pfizer's clinical trials. Partial reproduction of Figure 9 (A; cumulative incidence of COVID-19 among vaccinated and placebo groups) and of Figure 7 (B; neutralizing antibody titers on the day of the first injection [D1] and on various days thereafter) from the EMA assessment report [60]. Note the logarithmic $y$ axis in B. See text for discussion.

would imply that the first injection is enough to establish full immunity. This conclusion, however, is not stated, and in fact Pfizer does not report any data at all on test persons who received one injection only.

A sudden onset of full immunity on day 12 after the first exposure to the microbe or vaccine in question is not at all a biologically plausible outcome. Most of the trial participants are said to have had no evidence of prior COVID-19 infection. While many will have had some degree of cross-immunity, a full-blown specific immune response would have set in more gradually and slowly (compare Figure 2.10). Just such a pattern was indeed reported for this very same vaccine, in this very same clinical trial, in Figure 7 of the EMA report, which is reproduced here as Figure 2.13B. The figure shows the increase of neutralizing antibodies to SARS-CoV-2 before the first injection of the vaccine and at various time points thereafter.

Considering the foregoing, we should expect that the blood level of neutralizing antibodies should reflect the degree of clinical immunity to the virus. This is, however, not at all what we see in Figure 2.13B. On day 21 after the first injection, that is, a full 9 days after the sudden onset of full clinical immunity evident from Figure 2.13A, the amount of neutralizing antibodies in the blood has risen just barely above the background level. The maximal level of neutralizing antibodies is observed only on day 28 after the first injection, at which time most

test persons would already have had their second injection. The time course of cellular (T-cell) immunity was not reported, but in the absence of proof positive to the opposite it can be assumed to resemble that of the antibody response.

In summary, the sudden onset of full clinical immunity on day 12 after the first injection is highly implausible on its face, and the credibility of this claim is further undermined by the antibody studies conducted as part of the same trial. The claim must therefore be considered fraudulent. In this context, we also note that several individuals who had carried out contract work for Pfizer in the clinical trials spoke to the British Medical Journal about irregularities that had occurred in these trials. These included poor laboratory management, delayed and intentionally falsified data entry, and altogether missing follow-up examinations on symptomatic patients [61]. One of them summed it up as follows: *"I don't think it was good clean data ... It's a crazy mess."*

With Moderna's clinical trials, the situation is no better. For more evidence of data fraud by both manufacturers, see Palmer et al. [62].

# 3. Immunological mechanisms of harm by mRNA vaccines

We had seen in the preceding chapter that cells which express "non-self" antigens will be attacked and destroyed by our immune system. In viral infections, this is a necessary evil, because it leads to the elimination of the befallen cells. A mitigating circumstance is that most viruses target a limited spectrum of tissues and cell types, and most tissues can regenerate, so that wounds can heal thereafter.

Proponents of mRNA vaccines commonly argue that these agents do nothing more than mimic what happens in actual virus infections. Expression of the alien protein is thereby claimed to be short-lived and confined mainly to the site of intramuscular injection. Serious adverse reactions are therefore not to be expected. Nothing, however, could be more misleading and further from the truth.

## 3.1 mRNA vaccines are distributed throughout the body and prominently affect the blood vessels

The assertion that the mRNA/lipid nanoparticles remain at the site of injection is now widely known to be a blatant untruth. These vaccines rapidly spread from the site of injection to regional lymph nodes and to the blood circulation (see Section 5.2.1). Moreover, in contrast to most viruses, mRNA vaccine nanoparticles can be taken up by any cell type, including the *endothelia*, which form the innermost cell layer of the blood vessels.

The involvement of the endothelia immediately distinguishes mRNA vaccination from most naturally occurring infections. In Section 2.1, we noted that viruses depend on specific receptor molecules on the surfaces of their host cells, which limits the scope of cells and tissues they can infect. Very few viruses target endothelial cells, but those that do can cause dangerous hemorrhagic fevers; the Dengue, Ebola and Marburg viruses are examples. Intracellular bacteria that infect

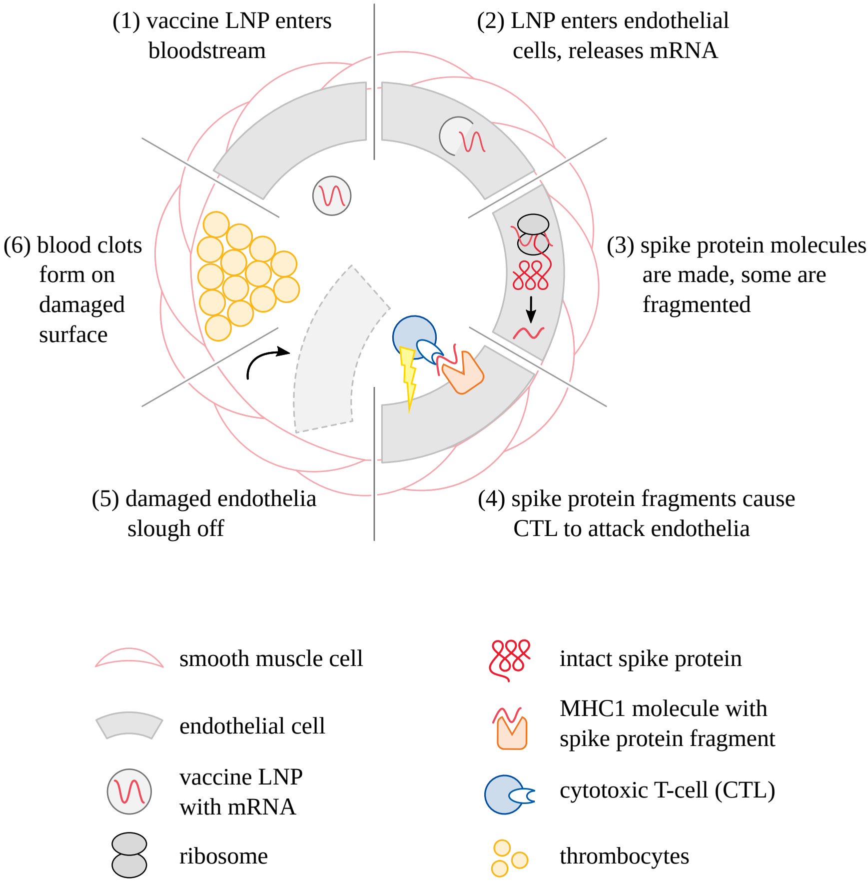



**Figure 3.1** How mRNA vaccines damage blood vessels and cause clotting. After the vaccine lipid nanoparticles have entered the circulation (1), they are taken up by the endothelial cells, and the mRNA is released (2). The antigenic protein (e.g. the SARS-CoV-2 spike protein) is then expressed (3) and transported to the cell surface, where it induces immune attack against the cells by antibodies and complement or by cytotoxic T-cells (4). Damaged endothelial cells slough off (5), which permits leakage of vaccine particles into the adjacent tissues. It also exposes the deeper layers of the vessel wall to the blood, which triggers thrombocyte aggregation (6) and blood clotting.

vascular endothelia also cause life-threatening disease (e.g. typhus and Rocky Mountain spotted fever). The clinical diseases caused by these pathogens are characterized by bleeding, often compounded by thromboembolic complications, which strikingly resembles some of the major acute adverse reactions to the COVID-19 mRNA vaccines.

With both the infectious hemorrhagic fevers and mRNA vaccines, the damage mechanism is quite straightforward: endothelial cells that express “non-self” antigens will come under attack by the immune system (Figure 3.1). As discussed earlier, this immune attack can involve antibody-mediated complement activation, cytotoxic T-cells, and other effector mechanisms in varying proportion. Blood clots forming in the wake of endothelial injury will result in circulatory disturbances, with sometimes grave and irreversible consequences like heart attack and stroke. The evidence on this point is unequivocal—the expression of the spike protein in the cells of the blood vessels, the ensuing immune attack on these cells, and the induction of blood clots are all clearly visible in tissue samples from biopsies and autopsies (see Section 4.3).

## 3.2 The expression of spike protein in the body is widespread and long-lasting

Studies on a model mRNA vaccine have shown that the lipid nanoparticles, after intramuscular injection, rapidly enter the bloodstream. They subsequently accumulate preferentially in certain organs including the liver, the spleen, and the ovaries. The factors which influence the accumulation of the vaccine particles in different organs will be discussed later (see Section 5.1). However, at least the blood vessels themselves are exposed to the vaccine in every organ and every tissue, from which we have to expect widespread expression of the foreign antigen. With the COVID-19 mRNA vaccines, such widespread expression has indeed been directly demonstrated; some of the evidence will be presented Chapter 4.

Another important consideration is how soon the antigen is expressed, and how long this expression lasts. Ogata et al. [63] have detected expression of the SARS-CoV-2 spike protein in blood samples even on the day of the injection. In this context, we should note that the spike protein may undergo cleavage by proteolytic enzymes (or proteases). This yields two fragments, called S1 and S2. The S2 fragment remains anchored to the cell surface, whereas the S1 fragment is released; it is this fragment which was detected in the blood samples by Ogata et al. The amount detectable in these samples peaked within the first week and then rapidly dropped. That short apparent duration, however, was likely due to the concomitant rise in the level of circulating antibodies. These antibodies would have bound to the antigen and

thereby interfered with the detection method, which itself relied on the capture of the antigen with specific antibodies.

Bansal et al. [64] reported another study on the time course of spike protein detectable in blood samples. In contrast to Ogata et al., they detected a rise only at two weeks after the initial vaccine injection. The highest levels were found at two weeks after the second injection. Even at four months after that second injection, however, Bansal et al. still detected considerable levels—similar to those detected after the initial two weeks. These authors' findings deviate from those by Ogata et al. in two respects: firstly, the antigen was detected after much longer time periods than reported by Ogata et al.; and secondly, Bansal et al. did not see Ogata's early peak.

These two discrepancies may be explained by the different sampling and assay methods used in the two studies. Ogata et al. applied their antibody capture assay to regular serum samples that had not undergone any prior processing. In contrast, Bansal et al. first isolated so-called *exosomes*—cell-derived membrane vesicles—from the serum, which they then examined by *Western blot*, i.e., the separation of proteins by SDS gel electrophoresis, followed by identification of the spike protein with antibodies.

With respect to the early expression of spike protein, there is reason to favor the data reported by Ogata et al., since they did not discard the fraction of spike protein which was *not* bound to exosomes. On the other hand, with regard to the late expression, the study by Bansal et al. is preferable, since their use of SDS gel electrophoresis should have removed the interference of serum antibodies with the detection of spike protein.

The upshot is that both the early expression reported by Ogata et al. and the late expression reported by Bansal et al. are credible. A more extensive discussion of both studies has been given elsewhere [65]. A fairly long-lasting expression of spike after mRNA vaccination was also reported by Röltgen et al. [66], who still detected the spike protein in lymph nodes 60 days after the second injection, and at this same time point also showed the continued presence of mRNA encoding the spike. Similarly, Magen et al. [67] detected strong spike protein expression and continued presence of the RNA at one month after vaccination. Their study concerned a patient with vaccine-induced myositis (muscle inflammation), and their tissue samples were taken from skeletal muscles located distantly from the injection site.

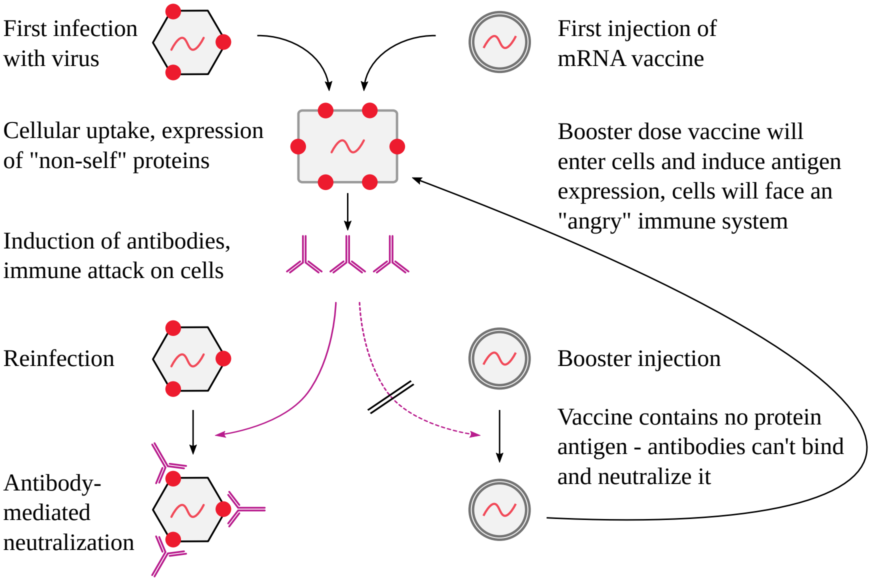



**Figure 3.2** mRNA vaccines fly under the immune system's radar. Left: the particles of a proper virus are decorated with some of the proteins which are encoded by the viral genome. As a consequence, the virus will efficiently enter cells only when we are first infected with it, whereas on subsequent encounters, antibodies induced after the first infection will neutralize the virus. Right: in contrast, mRNA vaccine particles don't contain any protein antigen; therefore, antibodies against the encoded protein antigen can't prevent the particles from entering our body cells and exposing them to immune attack.

Such long-lasting persistence of the mRNA, and therefore of antigen expression, must be assumed to be unrelated to the identity of the encoded antigen. Instead, it is most likely a property of the delivery technology in general. The calamitous consequences of this long-lasting antigen expression will be considered below.

## 3.3 The mRNA vaccine LNPs fly under the radar of the immune system

Another crucial difference between real viruses and mRNA vaccines is that the particles of the former, but not the latter, are decorated with copies of the protein molecules encoded by the nucleic acids contained in those particles. The consequences of this difference are illustrated in Figure 3.2.

We noted earlier that viruses typically cause significant disease only once, namely, when we are first infected with them; this is because at the first encounter we have no antibodies or other specific immune mechanisms yet which could prevent the virus from entering and multiplying within our body cells. However, after our first infection, we will have memory B-cells, which can meet any repeated infection with a rapid antibody response; the antibodies will then bind and neutralize the virus particles.

For this antibody-mediated neutralization to work, the particles of the virus must contain and expose at least some of the antigens encoded by it. That is indeed the case with all actual viruses. In contrast, the particles of an mRNA vaccine are encased with a shell of lipid molecules only, which are not effective antigens.[1] Therefore, even though the first injection with the vaccine will induce antibodies against the encoded antigen, those antibodies will be unable to recognize and neutralize the vaccine particles when another dose is injected. The vaccine will therefore enter our body cells with undiminished efficiency. Only when the antigen is expressed and appears on the surface of those cells will the antibodies recognize it; and they will now direct the full destructive force of the immune system against those cells.

The above assumes that the antigen does appear on the cell surface in intact form. This is indeed the case for the COVID-19 spike protein, but it may not apply with some future mRNA vaccine that encodes a different antigen which remains inside the cell. In this case, however, we must expect the antigen to be processed and presented in the form of MHC1-associated peptides; these would then attract the attention of cytotoxic T-cells. Thus, regardless of whether B-cells or T-cells dominate the memory response—the upshot is that prior immunity to the antigen encoded by the mRNA vaccine will *aggravate* the damage caused by repeated exposure to the agent. In keeping with this theoretical prediction, the risk of vaccine-induced myocarditis after the second mRNA vaccine injection reportedly exceeds that after the first one (see Li et al. [71] as well as Section 7.3).

In a nutshell, therefore, while specific immunity *mitigates* or entirely prevents disease caused by repeated virus infections, it will *worsen* the harm done by repeated injection of an mRNA vaccine. It bears mention

[1] Some individuals actually do have preexisting antibodies against some of the lipids, particular the ones which contain polyethyleneglycol (PEG). Such antibodies can cause allergic reactions to the vaccines [68–70].

that such prior immunity need not have been induced by a preceding vaccine injection; the effect will be much the same when someone who has previously been infected with the virus in question receives his first mRNA vaccine injection. Thus, in the context of the COVID-19 vaccinations, the authorities' refusal to exempt those with such natural immunity from their vaccine mandates has likely increased the number of severe adverse events substantially.

We also note that the problem discussed here is less acute with the adenovirus vector-based genetic vaccines. While with these vaccines, too, the antigen of interest is not part of the infectious particles, the antibody response triggered against the proteins of the adenoviral vector will tend to neutralize the vaccine virus particles upon repeated injection. This is, of course, not to be understood as an endorsement of the adenovirus vector technology; the virus-based vaccines against COVID-19 have caused severe adverse events on the same scale as the mRNA vaccines [72].

## 3.4 Induction of autoimmune disease

**3.4.1 Background.** We noted in the preceding chapter that autoimmune disease is caused by the emergence and proliferation of T- and B-lymphocytes which aberrantly recognize "self" antigens. Autoimmune diseases usually involve various degrees of cell and tissue destruction, which are brought about by the same effector mechanisms that exist for the sake of eliminating virus-infected cells. However, in some cases, the autoantibodies may cause more subtle functional disruption, such as the inhibition of signal transmission from nerve cells to muscle cells in myasthenia gravis, or the excessive activation of growth and hormone production within the thyroid gland in Graves' disease. In yet another paradigm, an autoimmune disease that is transient, though possibly protracted, nevertheless irreversibly damages organ function. A good example is the autoimmune aggression against the insulin-producing β-cells of the pancreatic islets, which results in type 1 diabetes, a lifelong condition.

As the above examples suggest, the self antigens which are the targets of autoimmune disease are often organ-specific. Another illustration is the protein thyroglobulin, which occurs only in the thyroid gland, and which is a key self antigen involved in this organ's destruction by an autoimmune disease known as Hashimoto's thyroiditis. Blood cells, too, can be targeted by autoimmune disease. For example,

some autoantibodies may destroy the thrombocytes (blood platelets), which are essential for blood clotting. The result will be "thrombocytopenic purpura", that is, spontaneous bleeding beneath the skin and in other places. Other autoantibodies may *activate* the thrombocytes, in which case blood clots will be observed. Their needless and excessive activation, too, will deplete the thrombocytes, so that the clinical picture may be a combination of clotting and bleeding. The latter has been observed after COVID-19 vaccination and termed "vaccine-induced thrombotic thrombocytopenia" (VITT).

Not all autoimmune disease is organ-specific, however. In some forms, the autoantigens are found throughout the body, which means that an autoimmune attack on them will afflict many different organs. A good example is systemic lupus erythematosus (SLE). Characteristic for SLE are antibodies against DNA and phospholipids, which are ubiquitous in all cells and tissues. As one might expect from the involvement of multiple organs, SLE is a very serious disease.

**3.4.2 Autoimmune disease induced by infections.** Most autoimmune diseases have a strong genetic component, but on the other hand almost all of them require some additional trigger to become manifest. Such triggers can be infectious agents. One example are group A streptococci, which can cause acute rheumatic fever. This autoimmune disease is again transient, but it can cause irreversible damage to the heart.

With acute rheumatic fever and several other autoimmune diseases, the central mechanism is believed to be *molecular mimicry* [73, 74]. In this pathogenetic mechanism, a non-self antigen of the infectious agent closely resembles one of the body's self antigens, so that T-cell or B-cell clones whose receptors recognize either of the two will also recognize the other. Such cross-reactive lymphocyte clones are already present before the infection strikes. However, at this stage, they are not active—instead, they are in a dormant state that was imposed on them by other, regulatory T-lymphocytes in order to safeguard the body cells that express the self antigen.

This somewhat precarious state of self-tolerance may break down when the infectious agent bursts onto the scene, and with it the cross-reactive microbial antigen. The infection will cause inflammation, which will provide the non-specific impetus for initiating an immune response (cf. Section 2.2.2.1). Among the many different T- and B-cell clones that will be recruited and activated by this response are the dormant

ones which recognized the cross-reactive microbial antigen. They will then attack not only the microbe but also the body cells which express the corresponding self antigen. Because of the delay inherent in any adaptive immune response, the autoimmune disease will typically flare up several weeks after the infection. For example, acute rheumatic fever may be diagnosed some 1-5 weeks after the usually trivial streptococcal infection that triggered it.

Molecular mimicry is also widely believed to occur in the pathogenesis of type 1 diabetes. Several viruses have been implicated, including Coxsackie viruses, cytomegalovirus, and rotaviruses. However, other mechanisms of causation, in particular a persistent infection of the pancreatic islet cells with the virus in question, also remain under consideration [75].

Various autoimmune phenomena and diseases have been reported in connection with COVID-19 infections and after vaccination against the disease [76, 77], and molecular mimicry has been suggested as a key mechanism [76, 78]. While this causation is conceivable in principle, the count of potential antigenic determinants which can be predicted by comparing the amino acid sequence of the SARS-CoV-2 spike protein to those of human proteins is very similar to the counts obtained with the spike proteins of other coronaviruses.[2] Thus, if SARS-CoV-2 is indeed "the autoimmune virus", as claimed by Halpert and Shoenfeld [76], then this must be ascribed to factors other than the abundance of cross-reactive immunological determinants.

**3.4.3 Deficient clearance of self antigens released from deceased cells.** We discussed in Section 2.2.1 that antigens which remain inside our body cells throughout their entire life cycle will only encounter the immune system after fragmentation and presentation by MHC1 surface molecules; they will not normally encounter antibodies. Keeping these antigens away from the cells which bring about the production of antibodies is an important aspect of self-tolerance. To maintain

[2]A published computational study has claimed that the SARS-CoV-2 spike protein has far greater sequence similarity, and therefore greater potential for immunological cross-reaction, with human proteins than with those of animals [79]. However, these purported findings extend even to chimpanzees, which are very closely related to humans. We could not reproduce these findings—neither does SARS-CoV-2 spike protein contain more sequence similarity to human than to chimpanzee proteins, nor does it exceed the extent of similarity observed with the spike proteins of several other coronaviruses. Thus, any unusually high propensity of SARS-CoV-2 to trigger autoimmunity is not accounted for by the number of predictable cross-reactive epitopes.

this separation, body cells which disintegrate must be cleared away promptly and in an orderly manner.

An important mechanism to ensure this orderly disposal of cell debris is *apoptosis*. When cells undergo programmed cell death, for example as the result of cytotoxic T-cell action, the cell fragments expose molecular markers which identify them to the scavenging phagocytes as derived from self. The phagocytes will then *not* respond as they would to the ingestion of a pathogenic microbe, and therefore will not activate T-helper cells to induce an antibody response.

If this orderly clearance mechanism is overloaded, and therefore the cellular debris is left to 'rot' before being removed, then it may no longer be recognized as derived from self. The phagocytes may then initiate the production of antibodies to 'hidden self' antigens contained in the debris (see Section 2.2.2.1). These autoantibodies will further promote inflammation, which will in turn destroy more cells and release more cellular debris; the final result of this vicious cycle may be full-fledged autoimmune disease. In keeping with this mechanism, a number of gene defects which interfere with the phagocytic clearance pathway promote the manifestation of SLE [80].

In principle, any tissue insult could potentially set in motion this pathway to autoimmunity; this includes infections, vaccinations, and apparently even physical trauma [81, 82]. In this context, we note that many participants of the COVID-19 mRNA vaccine clinical trials experienced high fever [83, 84]. Both the immunological mechanism of cell destruction and toxic activity of the lipid nanoparticles [85] may contribute to the inflammation underlying these febrile reactions. From such findings, we should expect autoimmune phenomena after vaccination to be common.

**3.4.4 Autoimmune diseases induced by COVID-19 vaccines.** The medical literature indeed contains numerous case reports of autoimmune diseases induced by COVID-19 mRNA vaccines. For organ-specific examples, see [86–89]; for a general overview, see [77]. The diagnoses include type 1 diabetes, thyroiditis, Guillain Barré syndrome, hepatitis, systemic lupus erythematosus (SLE), thrombocytopenic purpura (i.e. antibody-mediated blood platelet destruction), and many others. We will discuss some specific examples in Chapter 4.

## 3.5 Vaccine-induced immunosuppression

**3.5.1 Manifestations of immunosuppression after COVID-19 vaccination.** While autoimmune phenomena triggered by the COVID-19 vaccines have arrived in the mainstream of the medical literature, this is not yet the case with another potential consequence, namely, immunosuppression. The clearest indication of immunosuppression is provided by the numerous case reports of shingles occurring shortly after vaccination; for a large series of documented cases, see [90]. Shingles arises through the reactivation of varicella zoster virus (VZV). The initial infection with this virus causes chickenpox. While this is clinically a generalized but self-limiting disease, the virus stays behind in the sensory nerve nodes (ganglia) near the spinal cord. Most peoples' immune systems manage to keep the virus in check perpetually and prevent it from ever appearing on the scene again. However, in some persons, typically middle-aged or elderly, the virus can break out into the open once more to cause shingles. The skin lesions look like those in chickenpox, but their spread is typically limited to one *dermatome*, that is, the skin area which corresponds to a single sensory nerve node. A case of shingles may signal the presence of an underlying systemic disease that saps the immune system, and it is advisable to examine every shingles patient for further signs of such a disease.

In addition to shingles, bacterial infections, often involving the digestive tract, have also been reported after COVID-19 vaccination [91–93]. Such cases, too, might be caused by immunosuppression, but blood clots and disrupted perfusion of the affected sites may well contribute; based on the published reports, it is not possible to make a clear causal attribution.

Several experienced pathologists have shared their observations on rising case numbers and increased malignancy of cancers since the beginning of the COVID-19 vaccinations (see e.g. [94]). Many such cases seem to involve the reactivation of cancers, sometimes after decades, which had been considered cured. The mechanisms of cellular immunity that keep cancer cells in check are basically the same as those which control and combat viral infections. Therefore, these reports also point to significant immunosuppression after vaccination.

**3.5.2 Possible mechanisms.** As noted above, immunosuppression is not yet commonly acknowledged as a significant problem caused by the COVID-19 vaccinations, and we are not aware of any published

experimental research to address the question of its causation. However, several causative mechanisms are plausible (and not mutually exclusive).

**3.5.2.1 Saturated bandwidth.** The immune system is subject to global restraints on the extent of its activation. If its attention is focused on the sustained vaccine-induced expression of a foreign antigen in multiple tissues and organs of the body, this will divert resources from fighting actual pathogens which happen to invade concomitantly.

**3.5.2.2 Lymphocyte fratricide.** We discussed earlier that body cells which express the mRNA vaccine-encoded foreign antigen will be attacked by cytotoxic T-cells and by other cytotoxic immune effector mechanisms. Lymphocytes themselves are not exempt; if they take up the mRNA vaccine, they, too will become targets for other lymphocytes. In this manner, the immune system would destroy itself. Pathologist Arne Burkhardt has observed high levels of spike protein expression in lymph nodes and within the spleen, the body's largest lymphatic organ. This finding supports lymphocyte fratricide as an important mechanism of immunosuppression.

**3.5.2.3 Immunosuppression by lipid nanoparticles.** An immunosuppressive effect of the lipid nanoparticles has been demonstrated by Qin et al. [95]. These authors measured the lymphocyte activation and the antibody response to an experimental mRNA vaccine encoding an influenza virus antigen. This experimentally induced immune response was subdued by a preceding injection of lipid nanoparticles alone (and also of another experimental mRNA vaccine). Interestingly, the immunosuppressive effect was more pronounced when both injections were applied into the same body site, suggesting that damage to the regional lymph nodes by the first injection was partly responsible. However, changes to the pattern of immune responses were also observed when the second injection was applied to another body site, and remarkably were even passed on to the offspring of LNP-injected mice.

Lymphocytes are notable for their extraordinary sensitivity to apoptotic stimuli—for example, they can be driven into programmed cell death by very low doses of ionizing radiation. As we will discuss in Section 5.3.3.1, the toxicity of cationic lipids is mediated by reactive oxygen species, and the same is true of ionizing radiation. Therefore, lymphocytes might succumb to lipid nanoparticle toxicity more readily than other cells.

In this context, we might also note that in spite of their suppression of specific immunity, cationic lipids at the same time promote non-specific inflammation (see Section 5.3.2). This finding, as well as the inheritable changes of immune regulation documented by Qin et al., indicate that there is more to the LNP story than merely the killing of lymphocytes.

## 3.6 The fundamental mechanism of damage by mRNA vaccines is completely general

Since all of the evidence of harm discussed in this chapter relates to the COVID-19 mRNA vaccines, you might wonder what we should expect from future mRNA vaccines against other pathogenic microbes. Should we chalk up the toxicity of the COVID-19 vaccines to the specific antigen which they encode, or is such grievous harm inherent in the mRNA technology?

In our considered opinion, the outcome with any mRNA vaccine will be much the same as it was with the COVID-19 vaccines. It is true that the spike protein itself can promote blood clotting and inflammation without any help from the immune system [96]. Nevertheless, the evidence which will be shown in Chapter 4 indicates that the grave, widespread and sustained injury to tissues and to blood vessels is mostly caused by the immune attack on spike protein-producing cells. This attack occurs simply because the spike protein is a non-self antigen; and since every other mRNA vaccine will necessarily encode its own non-self antigen, derived from whichever particular microbe it targets, we must expect that it will cause harm by the same mechanism and to a similar extent.

# 4. Pathological evidence of immunological harm due to mRNA vaccines

Pathologists examine the organs and tissues of deceased patients, as well as tissue specimens of live patients (biopsies), in order to establish the causes of disease. While the macroscopic examination, at autopsy, of diseased organs is important and usually sufficient to diagnose causes of death such as lung embolism or myocardial infarction, much more detail can be revealed by the use of *histopathology*, that is, the microscopic examination of tissue samples. Microscopic study can be combined with biochemical and immunological techniques for detecting the occurrence and distribution of specific molecular markers of disease. Histopathology is useful not only in post mortem studies, but also with *biopsies*, that is, tissue samples obtained from living patients.

While pathological studies on patients who had suffered or died from adverse events of the COVID-19 vaccinations were slow to appear in the medical literature, there now is substantial evidence that sheds light on the mechanisms of disease causation. As we will see, immune attack on the body's own cells and tissues is the main recurring theme.

## 4.1 Key techniques used in histopathology

In order to examine a tissue sample under the microscope, it first needs to be cut into delicate slices of uniform thickness. In preparation for this step, the tissue sample is typically first treated with a *fixative*, often formaldehyde, and then embedded in paraffin. The fixative prevents chemical and structural degradation of the sample, and the paraffin firms it up for sectioning.

**4.1.1 Chemical staining.** Another important consideration is visual contrast. Most cells and subcellular structures are colorless, and not much detail is easily discernible under the microscope. To enhance contrast, the tissue samples are commonly stained with a mixture

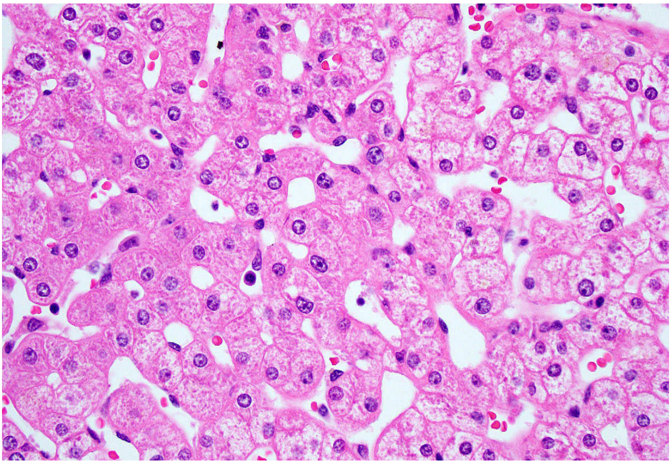


**Figure 4.1** Normal liver tissue (HE-stain). Cell nuclei are purple, whereas the remainder of the cell (the cytoplasm) is pink. In this image, we can see the outlines of most cells. That is not always possible, but one can always see the nuclei. The scattered little bright-red dots are red blood cells. They are located within empty spaces, the liver's *sinusoids*. In life, the sinusoids are entirely blood-filled; in this sample, however, most of the blood has been flushed out. Image adapted from [97].

of chemical dyes. Based on their ionic charges and other properties, these dye molecules will bind preferentially to different intra- and extracellular structures.

The widely used HE staining method uses the two dyes hematoxylin and eosin. The former is bluish and binds preferentially to nucleic acids and other negatively charged molecules, whereas the latter is red and preferentially binds to proteins. The usual result is that cell nuclei, which contain large amounts of DNA, appear blue or purple, whereas most of the remaining structures will be stained predominantly red (Figure 4.1). Deposits or droplets of fat remain unstained. While the HE method is useful for routine histopathology, there are a number of interesting special-purpose chemical stains which better highlight particular physiological or pathological cell and tissue structures.

**4.1.2 Immunohistochemistry.** An important technique that very substantially enhances the power of histopathology, and of which we will see several examples, is *immunohistochemistry*. It harnesses the specificity of antibodies for selectively staining cells which contain a particular molecule of interest. For example, while all lymphocytes

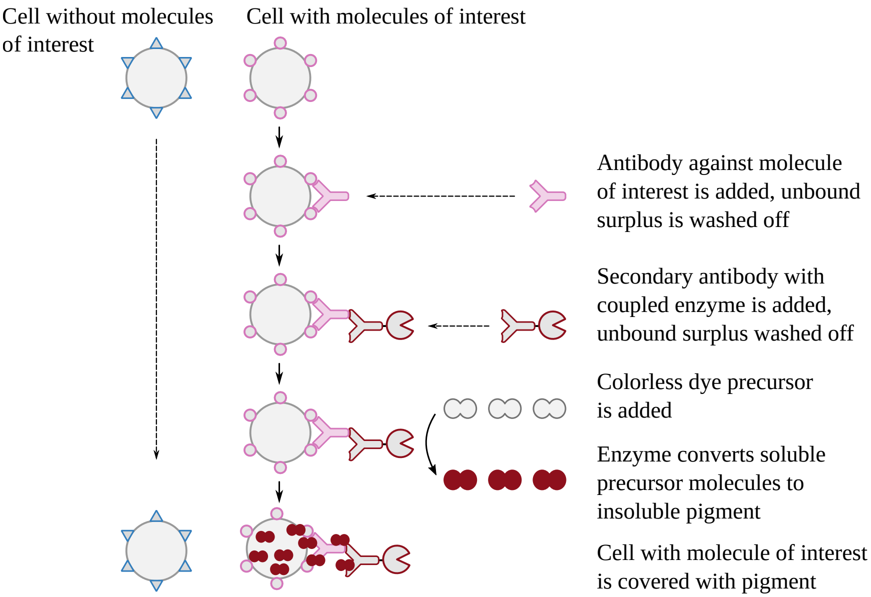



**Figure 4.2** Schematic illustration of immunohistochemistry, a method for selectively detecting specific molecules of interest in tissue samples using specific antibodies. See text for details.

look alike in the HE stain, immunohistochemical detection of the CD3 cell surface antigen can be used to highlight T- but not B-lymphocytes. Detection of CD4 and CD8, respectively, can be used to further distinguish T-helper from cytotoxic T-lymphocytes. And, as we will see, the expression of viral antigens such as the SARS-CoV-2 spike protein can be observed as well.

The essential steps of the method are illustrated in Figure 4.2. The tissue slice is first exposed to an antibody which specifically recognizes the molecule of interest. After allowing some time for binding to occur, the unbound surplus of antibody is washed off. A secondary antibody is then added which recognizes the first one, allowed to bind, and the unbound residue again washed off. This secondary antibody has been chemically coupled to an enzyme (a catalytic protein) which can convert a colorless, soluble precursor molecule (often diaminobenzidine) to an insoluble pigment which is deposited in situ.[1] This enzyme reaction

[1]One might wonder why the enzyme is chemically coupled to a secondary antibody rather than directly to the antigen-specific first antibody. This would indeed be possible in principle, but it is more convenient to couple the enzyme to a secondary antibody instead, since such a conjugate can be used with very many different antigen-specific

serves as an amplification step—a single enzyme molecule can turn over many dye molecules and thus generate a comparatively very large amount of pigment, so that even a small number of molecules of interest can be readily detected.

## 4.2 Sources of evidence

In the following, we will for the most part rely on case reports and reviews from the peer-reviewed medical literature. In addition, we will repeatedly reference a series of autopsy examinations carried out by Arne Burkhardt, MD, emeritus professor of pathology, with the assistance of several colleagues. While Burkhardt's results have not yet been published in the form of peer-reviewed journal articles, they have been demonstrated to and vetted by other pathologists and medical doctors, and they were available to the author of this chapter.

While most of Burkhardt's findings are qualitatively confirmed by those described in peer-reviewed articles, his work does add some valuable quantitative perspective. As of this writing, Burkhardt has evaluated autopsy materials from 43 patients who died after receiving one or more COVID-19 vaccine injections. In all of these cases, the diagnosis on the death certificate had *not* made reference to those vaccines, but the bereaved families had sought a second opinion from Burkhardt. His thorough investigation led Burkhardt to conclude that causation by the vaccine was certain or likely in 22 cases, and possible in 7 more cases. He ruled out causation in only 3 cases, whereas in the remaining 11 cases a conclusive determination could not or not yet be made.

Out of all 43 deceased patients, 29 were known to have received one or more injections of mRNA vaccines, but no others. Within this subset, Burkhardt deemed causation of death by vaccination certain or likely in 14 cases. Such figures should give pause to those who have thus far accepted the mainstream narrative that severe adverse events are "extremely rare."

## 4.3 Vasculitis induced by mRNA vaccination

In Section 3.1, we had discussed that the blood vessels will be prominently affected by vaccine damage, since the vaccines will initially be

primary antibodies, which need not themselves be chemically modified. For example, to detect cytotoxic T-cells rather than T-helper cells, we would simply replace the CD4-specific primary antibody with one that recognizes CD8; all other steps and reagents would remain unchanged.

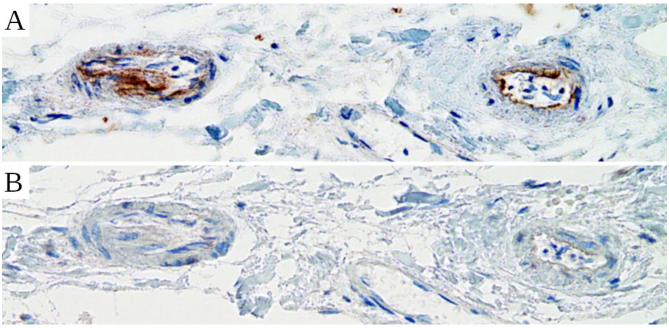



**Figure 4.3** Cross section of two small blood vessels located within the wall of a larger one (a coronary artery). Immunohistochemistry for SARS-CoV-2 spike protein (**A**) and nucleocapsid (**B**). Only the spike protein can be detected, indicating that its expression was caused by the vaccine rather than by an infection with the virus. Courtesy of Michael Mörz, MD.

distributed via the bloodstream; the cells of the vascular *endothelium*—the innermost layer of the vessel wall—will then take up the vaccine lipid nanoparticles and start expressing the spike protein. In this section, we will consider some supporting evidence.

**4.3.1 Vaccine-induced expression of spike protein in vascular endothelia.** Figure 4.3 shows the expression of spike protein within the endothelium of two small blood vessels, which are located within the wall of a larger one (a coronary artery). The brown pigment seen in panel A of the figure represents the spike protein. In panel B, immunohistochemistry was used in an attempt to detect the nucleocapsid of the SARS-CoV-2 virus. The absence of brown pigment indicates that the nucleocapsid is not expressed.

In an infection with the virus, *all* proteins encoded by the virus should be expressed and together, including both the spike protein and the nucleocapsid. On the other hand, the gene-based COVID-19 vaccines encode only the spike protein. The detection of spike protein alone therefore confirms that its expression was caused by vaccination rather than by an undiagnosed infection with the virus.

**4.3.2 Vasculitis, blood clots, and dissection: example autopsy findings.** Figure 4.4 shows HE-stained tissue sections from small and large blood vessels of people who died after COVID-19 vaccination. Panel A shows a cross-section through a normal artery. We see a sturdy, compact muscular layer, which displays a more intense red color than

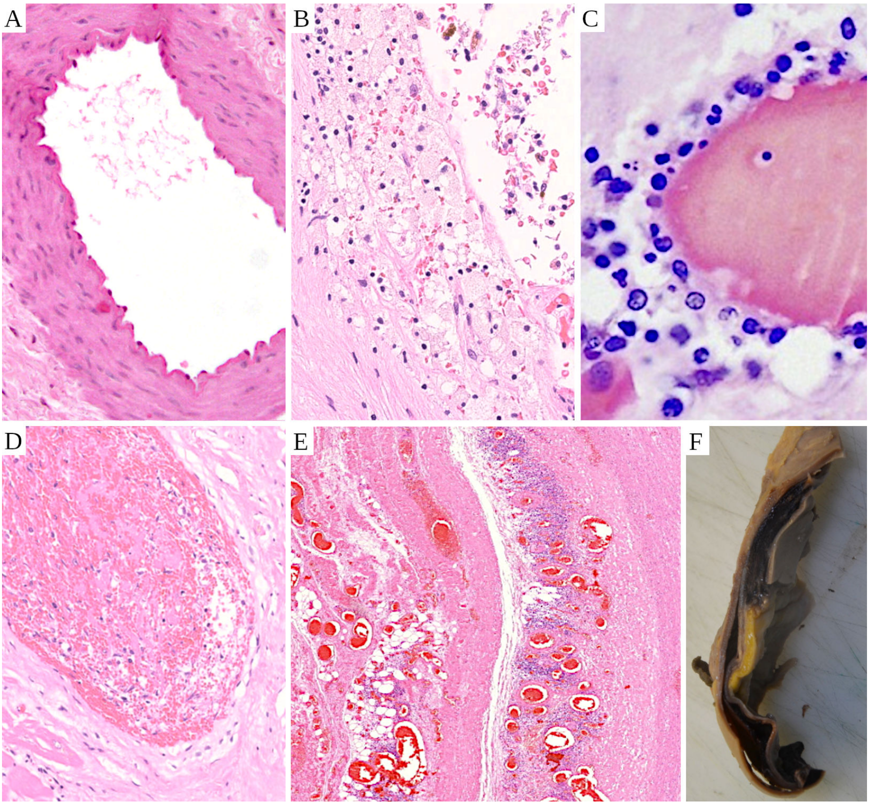



**Figure 4.4** Vasculitis of small and large blood vessels. Cross sections of a normal blood vessel (A), and manifestations of vasculitis after COVID-19 vaccination in small (C) and large (B, D, E, F) blood vessels. All microscopic section were HE-stained. **A**: a normal artery with a compact and regular muscular layer. The inner surface is unbroken and clearly defined; its wavy shape is a post-mortem artifact. **B**: the wall of an artery with vasculitis. The tissue is loosened up and “moth-eaten”; it has been invaded by lymphocytes (dark round dots) and macrophages. **C**: vasculitis of a smaller vessel (pictured at higher magnification). The vessel wall is infiltrated by both lymphocytes and granulocytes. **D**: vasculitis of a larger vessel has caused a blood clot, which fills the lumen. **E**: cross section of an aortic wall, shown at low magnification. Infiltrating lymphocytes appear as clouds of tiny blue specks. To the left of the largest blue cloud, a vertical crack runs through the tissue. **F**: a crack is also visible macroscopically in this excised specimen of aortic wall from a patient with *aortic dissection*. The dark material within the crack is coagulated blood. See text for further explanations. Image credits: panel A is from [97], B and D from Dr. Ute Krüger, C from Dr. Michael Möerz, and E and F from Dr. Arne Burkhardt.

the surrounding connective tissue. In the adjacent panel B, we see a wall section of a somewhat larger artery afflicted by vasculitis. Some muscle tissue remains intact at the bottom left, but most of the tissue has been infiltrated by inflammatory cells, including lymphocytes, and is disintegrating. Panel C shows a small blood vessel similarly affected; the higher magnification shows infiltration by lymphocytes and also granulocytes and histiocytes. Panel D shows another large vessel with vasculitis; the destruction of the wall is less advanced than in panel B, but it has caused the formation of a large blood clot, which entirely obstructs the lumen.

Panel E shows a wall section from the aorta of a vaccinated person. The image was taken at low magnification, and accordingly the infiltrating lymphocytes appear here as clouds of tiny blue specks. We see a crack running across the inflamed tissue. A crack is also visible macroscopically in panel F of the figure, which shows the same vessel as in E. The dark-colored material seen within in the crack is coagulated blood. This clinical picture is known as *aortic dissection*.

**4.3.3 Aortic dissection and rupture.** While dissection can occur in other arteries as well, it often affects the aorta, which is the largest blood vessel of the body. The aorta receives the highly pressurized blood ejected by the most powerful heart chamber (the left ventricle), and it is therefore subject to intense mechanical stress. If the wall of the aorta is weakened by inflammation, then it may fail under this strain. The failure begins with a rupture of the vessel's inner layer (the *intima*). The pressurized blood will force its way into the crack and from there into the underlying muscular layer, the *media*. As it pushes on, the blood splits the vessel wall into two separate sleeves. This zone of separation may spread along the entire length of the aorta and even beyond into its branches. If the outer sleeve of the damaged vessel holds, then prompt surgical treatment may save the patient, but if it bursts, then the ensuing internal bleeding will be immediately fatal.

Aortic dissection has previously been reported in connection with other forms of vasculitis [98, 99], and more recently also with COVID-19 infection [100, 101]. Aortic dissection and rupture are normally quite rare, but Prof. Burkhardt found three such cases in a total of 29 patients who had died after receiving an mRNA vaccine. (These three deaths occurred between 7 and 25 days after the most recent injection.) One of these cases was also studied by immunohistochemistry, and spike

protein was detected within the dissected segment of aortic wall. A Japanese group of pathologists has reported another such case [102].

The dissection and rupture of smaller arteries, sometimes facilitated by preexisting vascular malformations, has also been reported in multiple patients who had received a COVID-19 mRNA vaccine [103–107]. Prof. Burkhardt, too, found several such cases in his series of autopsies.

**4.3.4 Blood clots.** Vasculitis induced by mRNA vaccines has been found to affect all kinds of blood vessels, large and small; and so it is with the with blood clots induced by it. Figure 4.4D showed a blood clot in a larger vessel; several clots in smaller vessels are seen in Figure 4.5, which is taken from a case report by Roncati et al. [108] and shows tissue sections of the lung. In the right panel of the figure, we also see a large cluster of lymphocytes within the lung tissue itself. Similar observations were made by Prof. Burkhardt as well.

Aye et al. [109] surveyed 35 cases of myocardial infarction after COVID-19 vaccination; of these, 31 had received an mRNA vaccine. Most of these cases had occurred within 24 hours of the injection. The same is true of two cases reported by Sung et al. [110]; both patients had received the Moderna vaccine. Kawamura et al. [111] reports another case in connection with the Pfizer vaccine. Early manifestation is also apparent in the data collected by the VAERS database [112]; to what extent this is due to preferential reporting of such early cases is presently unknown. Myocardial infarction, most often in connection with underlying inflammation of the coronary arteries, was also a common observation in the autopsies reviewed by Prof. Burkhardt.

Kolahchi et al. [113] have published a review on acute ischemic stroke—i.e., stroke due to occlusion of a brain artery—in connection with COVID-19 vaccination. While the majority of the 43 patients included in their report had received an adenovirus-vector vaccine, there were eight patients who had been given an mRNA vaccine. Notably, five of these eight patients developed stroke already after their first vaccine injection, quite possible facilitated by preexisting natural immunity (cf. Section 3.3).

Another common clotting-related brain disorder is venous sinus thrombosis; here, a large vein rather than artery is obstructed by a thrombus. Like ischemic stroke, this disease has been more commonly observed with the viral vector vaccines, but again there have been case reports after mRNA vaccination as well [114–117].

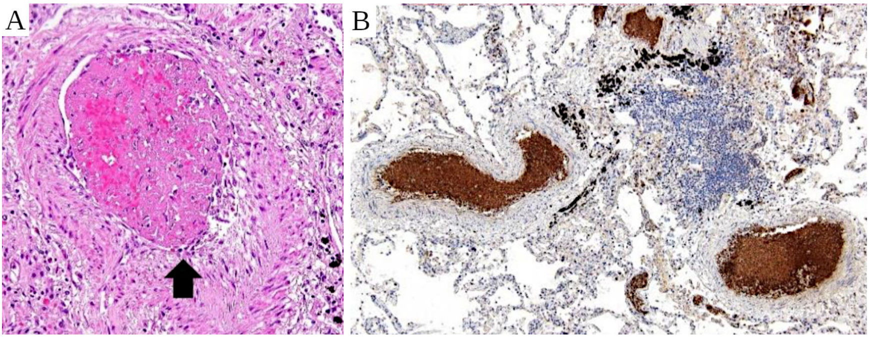



**Figure 4.5** Blood clots in lung tissue. **A:** a blood clot obstructs a small artery in the lung. The wall of the vessel shows signs of vasculitis. **B:** Several lung vessels obstructed by thrombi. The brown pigment was generated by immunohistochemistry, which detected platelet factor 4, indicating that the clots are rich in platelets (thrombocytes). The blue cloud to the right of the center is a large lymphocyte infiltrate. Figure adapted from Roncati et al. [108].

Arterial and venous occlusion have also been reported in many other anatomical locations; for example, Ahn et al. [118] reported a case of thrombosis of the inferior vena cava with lung embolism in a young patient who had received the Moderna mRNA vaccine. An elderly but otherwise healthy woman who developed similar manifestations after receiving the Pfizer vaccine was described by Scendoni et al. [119]. A dramatic, ultimately fatal case of multiple arterial occlusions within the gastrointestinal tract was reported by Lee et al. [120]. Multiple cases of arterial and venous occlusion with severe consequences were also found by Prof. Burkhardt in his series of autopsies.

**4.3.5 Variability of vasculitis.** In the foregoing, we saw examples of inflammation affecting the inner layer of blood vessels, which will be particularly likely to cause clots, as well as to the muscular middle layer (the media) of major arteries, which may lead to dissection and rupture. In other cases, the inflammation may primarily focus on the outermost layer of a blood vessel (the *adventitia*). All three vascular layers may be affected at different sites in one patient. Burkhardt found vasculitis in one or more vascular layers in 24 deceased patients out of 29 overall who had been injected with mRNA vaccines exclusively, and in 37 out of 43 genetically vaccinated patients overall.

The underlying pathogenetic mechanism which induces vasculitis is also somewhat variable. The immune attack may be carried out pri-

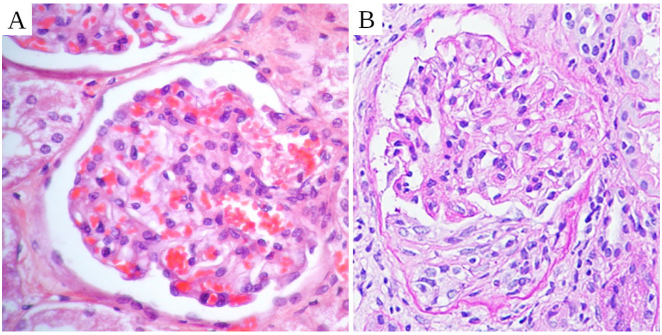



**Figure 4.6** IgA nephropathy after mRNA vaccination. **A:** a normal glomerulus [97]. It consists of a coiled arteriole, whose walls function as an ultrafiltration membrane. The filtrate is captured within the surrounding empty space, which is enclosed by *Bowman's capsule*. **B:** a glomerulus in IgA nephropathy after mRNA vaccination [122]. The lower third of Bowman's capsule is filled with proliferating cells as a result of inflammation.

marily by lymphocytes, or antibodies and complement may dominate. In the latter case, one may also see pronounced infiltration with neutrophil or eosinophil granulocytes and with macrophages (histiocytes). Mixed infiltrates including all of these inflammatory cell types are not uncommon.

Another possible variation is IgA vasculitis. This is a peculiar form of autoimmune disease, in which immunoglobulin A, one of the major antibody variants (see Section 2.7), functions as the autoantigen. In individuals genetically predisposed to the disease, formation of the autoantibodies directed against IgA may be triggered by microbial infections or by vaccinations [121]. Circulating immune complexes consisting of IgA and autoantibodies to it may be deposited in the kidneys, and more especially inside the kidney *glomeruli*, which carry out lateral flow filtration of the blood plasma as the first step of urine production. The result will be *IgA nephropathy*. Abnormal cell proliferation will be seen within the normally fluid-filled space that surrounds each glomerulus (see Figure 4.6). The ensuing functional damage to the filtration apparatus may cause blood cells or plasma proteins to appear in the urine.

Another manifestation of IgA vasculitis, which may occur alone or together with the nephropathy, are characteristic skin rashes, with blood seeping from damaged small vessels into the connective tissue layer of the skin. Two such cases which occurred after mRNA vac-

cination were reported by Nakatani et al. [122] and by Sugita et al. [123].

**4.3.6 The role of spike protein toxicity in vasculitis and clotting.** We have so far focused our discussion of the pathogenesis on the immune response to spike protein as a foreign antigen. Additionally, however, the spike protein is endowed with intrinsic toxicity. A remarkable variety of toxic activities have been ascribed to it, including for example injury to the blood-brain barrier [124, 125] and inhibition of DNA repair [126].[2] However, in the context of vascular damage, the main concern is the binding of spike protein to the ACE2 receptor, which occurs on many cell types, including both endothelial cells and blood platelets. Such binding will inhibit the enzymatic activity of ACE2 itself, which will promote blood clotting and possibly also inflammation [96].

As discussed in Section 3.2, the S1 fragment of the spike protein can been detected circulating in the bloodstream for a few days after mRNA vaccination; levels then drop quickly as antibodies to the protein appear [63, 131]. Presumably, those antibodies will inhibit not only the detection of the circulating spike protein but also its activity. Thus, a causal contribution of direct spike protein toxicity is the most likely in adverse events which occur within a few days after vaccination, especially in those patients who received their first vaccine injection and who had no preexisting natural immunity. Heart attacks and stroke are particularly common in this period. Adverse events which become manifest after the immune response to the spike protein has set in are more likely to be caused mainly by this immune response.

## 4.4 Immune attack on organ-specific cells and tissues

While vasculitis and clotting can cause damage to any and all organs, there is also evidence of more direct damage to organ-specific cells. In some cases, this has been linked to the expression of spike protein in such cells; examples are muscle cells in heart and skeletal muscle, lymphocytes in the spleen, and glia cells in the brain. However, so far only very few published case reports have attempted to detect the spike protein within tissue samples from patients injured by mRNA vaccines.

[2] On the website of the journal *Viruses* that had published it, the cited study by Jiang and Mei [126] is flagged as "retracted." However, the scientific reasons given for this "retraction" are unconvincing; it came about most likely through political pressure behind the scenes. There have been several similar instances of scientifically baseless "retractions" of COVID-related articles [127–130].

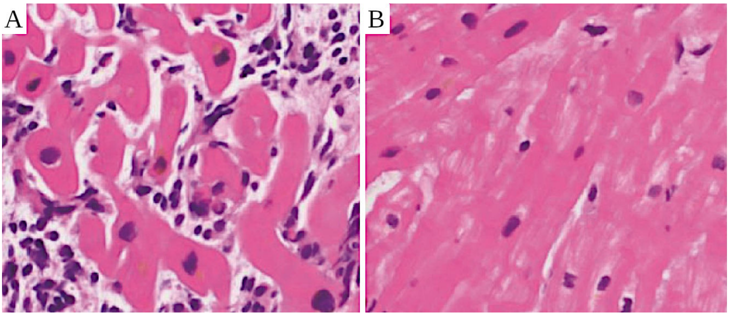



**Figure 4.7** Heart muscle biopsies from a case of myocarditis after mRNA vaccination. **A:** in the acute stage (8 days after vaccination), lymphocytes and other inflammatory cells are seen between the heart muscle cells. **B:** 58 days after vaccination, the inflammation has receded. Images adapted from Koiwaya et al. [132].

Accordingly, with most organs it is currently unknown to what extent the organ-specific cells may express spike protein. As with vasculitis, true autoimmunity that is triggered by vaccine-induced inflammation is an alternate or contributing mechanism of organ damage.

In the following, we will discuss several significant and instructive pathological studies on organs whose involvement has been repeatedly observed, without however striving for completeness.

**4.4.1 Myocarditis.** Expression of spike protein in heart muscle cells after COVID-19 vaccination has been documented in heart biopsies of myocarditis patients by Baumeier et al. [133]. Both mRNA and adenovirus-based vaccines were represented among the reported cases. More widespread and apparently stronger expression than reported by Baumeier et al. was detected by Burkhardt and colleagues in tissue samples from an as yet unpublished fatal case of myocarditis. Here, nucleocapsid expression was also examined but found to be negative, confirming that the expression of spike had been caused by vaccination.

As with vasculitis, the histopathological picture of myocarditis is fairly varied. The inflammatory cells invading the muscle tissue typically comprise multiple forms, but in some cases lymphocytes predominate (see Figure 4.7), whereas other cases show mainly granulocytes and histiocytes (see Figure 4.8). Several cases with a strong presence of eosinophil granulocytes were reported as well [134, 135].

The lymphocytes, where present, are predominantly T-cells; among these, cytotoxic T-cells were predominant in at least one case, as ap-

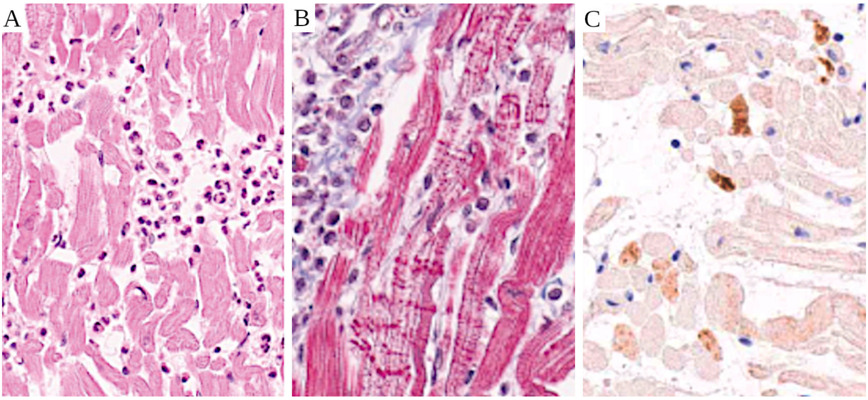



**Figure 4.8** A case of rapidly fatal myocarditis after mRNA vaccination (histopathology after autopsy). **A:** neutrophil granulocytes and histiocytes (macrophages) infiltrating the heart muscle tissue. **B:** horizontal red stripes indicate cell death of heart muscle cells (contraction band necroses). Masson's trichrome stain. **C:** deposits of complement factor C4 on heart muscle cells (immunohistochemistry). All images adapted from Choi et al. [136].

parent from the expression of the CD8 cell surface antigen typical for these cells [47]. Inflammatory infiltrates that show predominantly granulocytes and histiocytes are compatible with an immune response that is driven primarily by antibodies and complement, both of which provide chemotactic (i.e. attracting) signals to these inflammatory cells. In keeping with this interpretation, the case reported by Choi et al. [136] showed not only inflammatory infiltrates rich in neutrophil granulocytes and histiocytes but also the activation and deposition of complement proteins on the surface of damaged heart muscle cells (Figure 4.8C).

The most straightforward explanation for this finding is that these cells had expressed the spike protein; antibodies binding to the spike molecules then triggered complement activation. In this context, it is noteworthy that the pore formed by the complement membrane attack complex will admit extracellular calcium into the cell. Intracellular calcium excess is an acknowledged cause of contraction band necrosis, which was a prominent feature in the histopathology presented by Choi et al. (see Figure 4.8B). We must note, however, that Choi et al. did not attempt to demonstrate this mechanism, nor did they comment on the question of how complement activation had occurred.

A similar pattern of inflammation was reported by Gill et al. [137] in two fatal cases of myocarditis after mRNA vaccination. These authors suggest that their findings "resemble catecholamine injury" to the heart. The term "catecholamines" comprises epinephrine, norepinephrine, and dopamine. Disease states with excessive catecholamine release—in particular, tumors of the adrenal glands which produce epinephrine and norepinephrine—may indeed cause damage to the heart, but the connection suggested by Gill et al. is tenuous, considering the fatal outcome in these two previously healthy young men. We propose that the pathological findings reported by Gill et al. are more readily explained by antibody-mediated immune attack on spike-expressing heart muscle cells. This question deserves to be more thoroughly elucidated in future histopathological studies.

In a recently reported case that exhibited both encephalitis and myocarditis, inflammatory changes in the heart were mostly centered on the small blood vessels, which were also shown to express spike protein [138]. However, even where these small vessels had not been obstructed, damaged muscle cells with contraction bands (cf. Figure 4.8B) were also seen. This illustrates that vasculitis and direct inflammatory damage to organ-specific cells are not mutually exclusive.

In conclusion, the histopathological picture of vaccine-induced myocarditis shows considerable variation. Lymphocytic inflammation most resembles myocarditis caused by viruses, which before the arrival of gene-based vaccines were the predominant cause of this disease. Inflammation with predominant infiltration by granulocytes and other types of cells that are attracted by complement activation is compatible with an antibody-mediated immune response to spike protein expression. The collective evidence of cell and organ damage available so far seems consistent with the major immune effector mechanisms outlined already in Section 2.2.1; however, more in-depth investigations are needed to fully elucidate the immunological mechanisms underlying the varying patterns of inflammation.

**4.4.2 Lung inflammation (pneumonitis).** The lungs are prominently affected not only in severe cases of COVID-19 [11], but also by adverse events after vaccination. The former is unsurprising, since SARS-CoV-2 is a respiratory virus. With vaccination, one reason for their frequent involvement may be that the lungs constitute the first capillary bed which the vaccine particles will encounter after entering the blood-

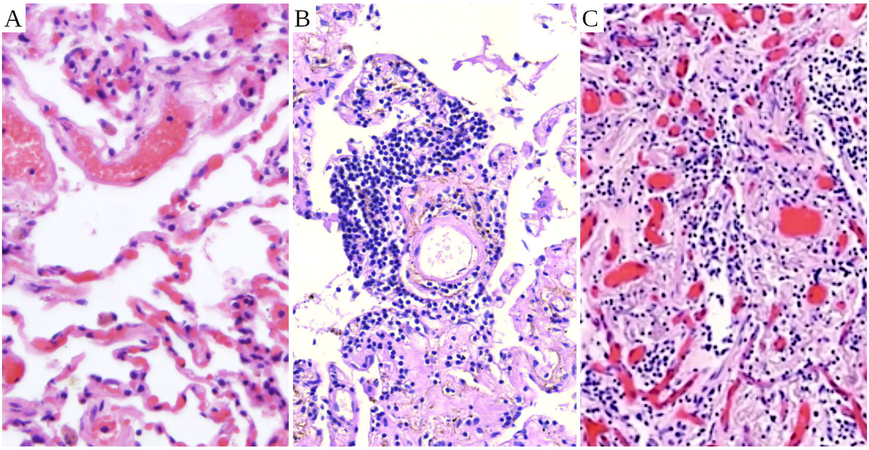



**Figure 4.9** Normal lung tissue (**A**), and lung alveolitis (**B**, **C**) after mRNA vaccination (Moderna). In **A**, we see air-filled spaces (the alveoli), delimited by delicate alveolar septa with embedded, blood-filled capillaries. We also see several somewhat larger blood vessels. In **B**, we see dense lymphocyte infiltrates. The septa are thickened by fibrosis (scar tissue). Fibrosis is even more advanced in panel **C**, where air-filled spaces have almost entirely disappeared. Panel A from [97]; panels B and C courtesy of Prof. Burkhardt.

stream. Moreover, thrombi that form within large veins in the periphery and then become detached will be carried through the bloodstream to the lungs, where they will get stuck; this is what we refer to as lung embolism.

Burkhardt noted some form of lung involvement in 17 mRNA-vaccinated patients out of 29 overall. While some of these cases were indeed caused by embolism or the local manifestations of vasculitis, infiltration by lymphocytes and inflammation of the lung tissue itself was noted in eleven cases. Inflammatory lung disease that is not caused by infectious agents is referred to as *pneumonitis*; if the inflammation centers on the alveoli, then the term *alveolitis* is also used.

Figure 4.5B above already showed an example of lung tissue infiltrated by lymphocytes. One of Burkhardt's cases is illustrated in Figure 4.9. This patient was a 80 years old woman, who had received the second of two doses of the Moderna vaccine 40 days before her death. In addition to the inflammation in the lungs, this woman was also suffering from myocarditis; both were most likely the leading causes of her death. In the figure, we see abundant infiltration of the lungs with lymphocytes. We also see *fibrosis*, i.e. the formation of scar tissue

induced by inflammation, which has thickened the septa between the alveoli to such a degree that little air-filled space remains between them.

A case of mRNA vaccine-induced pneumonitis with similar, but somewhat less severe histopathological findings in a lung biopsy was reported by So et al. [139]. Importantly, their patient survived and recovered after treatment with corticosteroids. Shimizu et al. [140] have described three clinically similar cases, but performed no biopsies; their report presents only radiological images.

A peculiar form of lung involvement that has been reported several times after mRNA vaccination [141–143] is known as *radiation recall pneumonitis*. This is a rare condition that may befall patients who have previously received radiation treatment of the lungs. Irradiation itself, in high doses, is sufficient to trigger pneumonitis, but this will typically heal, often with some degree of fibrosis. When such patients subsequently receive certain drugs, then the inflammation may flare up again in the previously irradiated area.

The drugs that have so far been known to evoke this condition are mostly cytotoxic anti-cancer drugs. A novel variation on the theme is the occurrence after use of certain monoclonal antibodies that are used therapeutically to enhance immune responses to cancer cells [144]. While the mechanism by which the COVID-19 mRNA vaccines cause this surprising reaction remains to be elucidated, the effect hints at interactions of these vaccines with the immune system whose nature is not yet understood.

**4.4.3 Brain inflammation (encephalitis).** Brain tissue includes two major cell types, the *neurons* (nerve cells) and the *glia cells*. The nerve cells are of course central to brain function, but the glia cells—a heterogeneous bunch—serve in many indispensable supporting functions. One of these is the formation of the *blood-brain barrier* (BBB), which they effect jointly with the vascular endothelia. The BBB protects the brain from many poisons carried by the bloodstream. It is, however, probably not of equally great importance in connection with mRNA vaccine nanoparticles; this is discussed in more detail in Section 5.1.3.

The forms of damage to the brain observed after COVID-19 vaccination resemble those also seen with other organs: vascular inflammation and occlusion, direct immune attack, and autoimmune disease. We will here focus on the latter two pathogenetic mechanisms.

**4.4.3.1 Encephalitis due to an immune reaction against spike protein.** If vaccine particles manage to leave the blood vessels and be taken up by cells in the surrounding brain tissue, then we must expect the immune system to attack and destroy those cells. How might it be proven that this has occurred in a given case of encephalitis? The following criteria would make such a diagnosis at least highly likely:

1. clinical manifestation within days to a few weeks of the vaccine injection;
2. detection of lymphocytes and other inflammatory cells within brain tissue;
3. detection of spike protein within the foci of inflammation.

It should be noted that criteria 2 and 3 can only be satisfied by histopathological examinations. With the brain, these are usually performed only after autopsy, since biopsies on this organ are of course particularly precarious.

While this mechanism may very well be of great importance, the supporting evidence so far is scant, because pathologists have not been looking for it. However, a first case report that fulfills all of the above criteria has recently been published [138]. Some of the findings are reproduced here in Figure 4.10. This very meticulous study also ruled out that the detected expression of spike protein was caused by infection with the virus itself rather than by vaccination, by using the nucleocapsid negative control discussed in Section 4.3.1.

The patient in question had initially received a single injection of AstraZeneca's adenovirus-based vaccine, followed by two injections of Pfizer's mRNA vaccine. The last injection had been given seven months after the first and three weeks before the time of death. Marked expression of the spike protein, likely caused in the main by the most recent dose of mRNA vaccine, was detected in the brain capillaries and also in some of the surrounding the glia cells. It must be noted that, even though neurons underwent cell death in numbers, they were not shown directly to express the spike. There seem to be three possible explanations:

1. the neurons did express the spike protein and therefore were directly attacked by the immune system, but their death interfered with the detection of the spike;

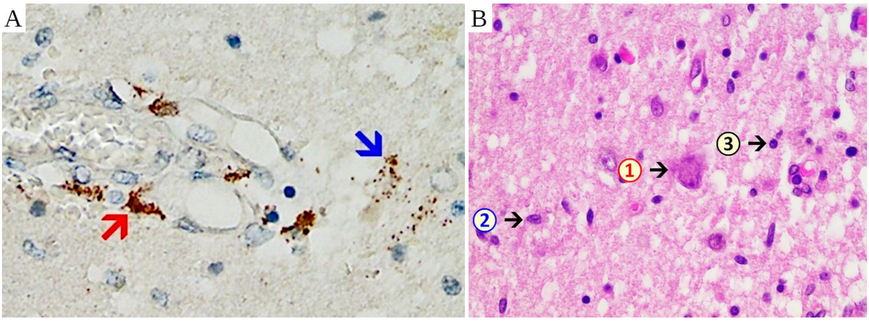



**Figure 4.10** Histopathology of encephalitis. **A:** Detection of SARS-CoV-2 spike protein by immunohistochemistry, within the wall of a small blood vessel (red arrow) and within several glia cells of the surrounding brain tissue (blue arrow). **B:** an encephalitic focus (HE staining). 1: a necrotic nerve cell; the cell nucleus has vanished. 2: a microglia cell; this cell type is more prevalent than usual. 3: a lymphocyte. Images adapted from a case report by Mörz [138].

2. the neurons expressed the spike protein, but antigen expression on the surface was mostly in the form of MHC1-associated processed peptides; or
3. the neurons did not express the spike protein and were not directly attacked, but rather were killed as bystanders in the general mêlée of the inflammation.

The second alternative may seem contrived, but it has been substantiated in principle by a study on liver tissue (see Section 4.4.6 below). It would seem worthwhile to determine its validity with brain tissue through further studies.

**4.4.3.2 Autoimmune encephalitis.** In this pathogenetic mechanism, the connection between encephalitis and vaccination is less immediate: the vaccine first triggers an inflammation, which might not even have to directly affect the brain; and in the context of this inflammation an immune response is triggered not only against the spike protein but also against one or more of the body's own proteins or other biomolecules (autoantigens; see Section 3.4). The immune system may then attack these same autoantigens within initially unaffected target organs, which may include the brain, and trigger inflammation here as well.

The clinical symptoms, and also the autopsy findings obtained with routine methods, will likely be very similar as with a direct immune

reaction to the spike. Therefore, how might one decide whether the encephalitis is triggered by the spike protein or rather by an autoantigen? In a true autoimmune encephalitis, one should expect the following findings:

1. autoantibodies to the autoantigens in question should be detectable in blood samples;
2. the spike protein should *not be* detectable in the inflammatory lesions;
3. the temporal connection to the vaccination might be less close, because autoantigens are produced in the body perpetually.

Jarius et al. [145] reported a case of autoantibody-positive encephalitis in a patient who had initially received two doses of AstraZeneca's adenovirus-based vaccine, followed by one dose of Pfizer's mRNA vaccine. In this patient, the autoantigen was a protein expressed in the brain—*myelin oligodendrocyte glycoprotein* (MOG). These authors also provided an overview of twenty previously reported cases that involved the same autoantigen. In three of these cases, an mRNA vaccine had been used, whereas the remaining seventeen cases were associated with the AstraZeneca vaccine. Since none of these cases were fatal, no positive or negative histopathological evidence of spike protein expression in the inflammatory brain lesions was obtained.

Asioli et al. [146] reported four cases of encephalitis in which autoantibodies against the LGI1 protein were detected. Three of these cases, all from the same Italian city (Bologna), occurred after injection of mRNA vaccines. A particularly striking case that involved brain inflammation was reported by Poli et al. [147]. This patient developed three different autoimmune diseases simultaneously—demyelinating encephalitis, myasthenia gravis, and thyroiditis. However, no specific autoantibodies were detected that could account for the encephalitis in this case.

**4.4.3.3 Antibody-negative autoimmune encephalitis.** This diagnosis was made in several case reports of encephalitis after injection of mRNA vaccines [148–150]. It is certainly reasonable to assume that some such cases may have been caused by unidentified autoantigens. On the other hand, without histopathology, it will often be impossible to decide whether a given case was caused by an immune reaction against an unknown autoantigen or against the vaccine-encoded spike protein.

Overall, while both direct immune response to spike protein and true autoimmunity have been substantiated as causes of post-vaccination encephalitis, their respective contributions to the overall incidence of the disease cannot be discerned from the limited available evidence.

**4.4.4 Liver inflammation (hepatitis).** Compared to most other interior organs, the liver is quite frequently affected by inflammation, which may be due to infectious or non-infectious causes. A brief overview of the various forms will provide useful background for judging the evidence of hepatitis induced by mRNA vaccines.

**4.4.4.1 Viral hepatitis.** There are several hepatitis viruses, transmitted either through the oral route (most commonly hepatitis A virus) or through contaminated blood or needles (hepatitis B and C viruses). Hepatitis A is typically acute and self-limiting. Hepatitis B and C may be transient, too, but in some patients they take a chronic course, which may progress all the way to liver cirrhosis and to organ failure.

**4.4.4.2 Toxic hepatitis.** The liver has a central role in the metabolic degradation of drugs and poisons. The intermediates which arise along these degradation pathways can be chemically quite reactive and give rise to toxic hepatitis. The most common case in practice is toxic hepatitis induced by alcohol, whose degradation gives rise to acetaldehyde as the reactive intermediate. In its early stages, toxic hepatitis is usually reversible upon withdrawal of the causative chemical agent.

**4.4.4.3 Autoimmune hepatitis.** This form of hepatitis is caused by an immune reaction to autoantigens which occur in liver tissue. Usually, multiple autoantigens are involved, and antibodies to these autoantigens are found in the blood. Most of the autoantigens in question occur not only in the liver but also in other tissues. Nevertheless, the disease typically affects the liver only, which must be due to some additional factors, either genetic or extrinsic in nature.

A hallmark of true autoimmune hepatitis is its protracted clinical course—since the inflammation is not driven by a virus that may be cleared, nor by a drug that may be withdrawn, the disease tends to linger and relapse.

**4.4.4.4 Autoimmunity in viral and toxic hepatitis.** While in theory the above forms of hepatitis can be neatly classified according to the cause, in practice there is considerable overlap. This is well illustrated

by several studies which appeared shortly after the discovery of the hepatitis C virus (HCV): a sizable proportion of patients who had previously been diagnosed with autoimmune hepatitis were now found to harbor HCV, which was in many cases deemed causative for the disease [151–153].

We already discussed earlier how infectious pathogens can promote autoimmune disease both through tissue damage and trough cross-reacting antigens (Section 3.4.2). Tissue damage is bound to occur in viral hepatitis. As noted above, toxic hepatitis is caused by reactive drug degradation intermediates, which also will inflict cell and tissue damage. Moreover, such intermediates may attach themselves to self antigens, which are thereby altered and made to look like non-self to the immune system. This may then lead to an immune response which is directed against the chemically altered antigen, but which may also extend to its unmodified self antigen precursor. Thus, in many cases of viral and of toxic hepatitis, autoantibodies of some sort are also present; but these are considered a *consequence* rather than the cause of the observed inflammation.

It follows that detection of autoantibodies alone cannot reliably tell true autoimmune hepatitis from viral or from drug-induced forms of the disease. Furthermore, immune attack on liver cells will produce similar histopathological effects regardless of whether it is triggered by self, modified self, or genuine non-self antigens.

**4.4.5 What effects on the liver should we expect with mRNA vaccines?** In Chapter 5, we will discuss how mRNA vaccines, after intramuscular injection, may distribute within the body. For now, we simply note that, among all organs, the liver accumulates the most vaccine particles per unit weight of tissue, aside from only the injection site itself. At these high tissue concentrations, the synthetic cationic lipids contained in the vaccine nanoparticles are likely to cause some cell and tissue damage. Liver cell damage was indeed observed in animal trials by both Pfizer [60, p. 55] and Moderna [154, p. 49]; and according to the report by the European Medicines Agency [60], Pfizer's own experts attributed it explicitly to the company's proprietary and previously untested cationic lipid.

We had seen above that triggering an effective immune response requires both a non-specific "danger" signal and a specific antigen (see Section 2.2.2.1). The cytotoxic effects of the cationic lipids can provide

the non-specific signal [85]. Translation of the mRNA into the spike protein would, of course, provide an effective target antigen. With these two stimuli, the stage is set for a vigorous immune response that will attack the liver cells. The ensuing inflammation will amplify the tissue damage and promote secondary immune responses to self antigens, i.e. autoimmunity. Thus, we might expect autoantibodies in at least some of the clinical cases.

That leaves the question of disease duration. While the manufacturers' and regulators' assurances of vaccine mRNA expression lasting only for days were overly optimistic (see Section 3.2), expression should indeed be transient. Thus, much like a case of toxic hepatitis, which will abate upon withdrawal of the drug that caused it, vaccine-induced inflammation should wane as expression of the mRNA subsides. Furthermore, we may expect that the inflammation will respond to immunosuppressive treatment with corticosteroids, as is the case with toxic hepatitis, and also with some reported cases of vaccine-induced encephalitis and pneumonitis (see above).

**4.4.6 Evidence of vaccine mRNA and its expression in post-vaccination hepatitis.** The number of published case reports on hepatitis after vaccination is rather high, but most of these studies do not provide molecular detail from which one could infer the pathogenetic mechanism. Two case reports stand out in this regard. The first one, published by Martin-Navarro et al. [155], describes the detection of vaccine mRNA in a liver biopsy through in situ hybridization. The mRNA is found in abundance throughout the entire tissue specimen that was examined. The study did not attempt to measure translation of the detected RNA into spike protein.

The second study [156] continues where the first one left off—it demonstrates the expression of spike protein in these liver cells, but indirectly and with an interesting twist: it shows the presence in the liver tissue not of spike itself, but rather of cytotoxic T-lymphocytes (CTL) specific for this protein; or more precisely, specific for a certain small peptide that will arise from the spike protein's intracellular fragmentation (see Section 2.2.2.2). The authors also tried to detect the presence of intact spike protein by immunohistochemistry, but the result was negative. A similar, not formally published finding was also shared previously in a presentation by Prof. Burkhardt, who had observed an at best weakly positive signal of the spike's expression

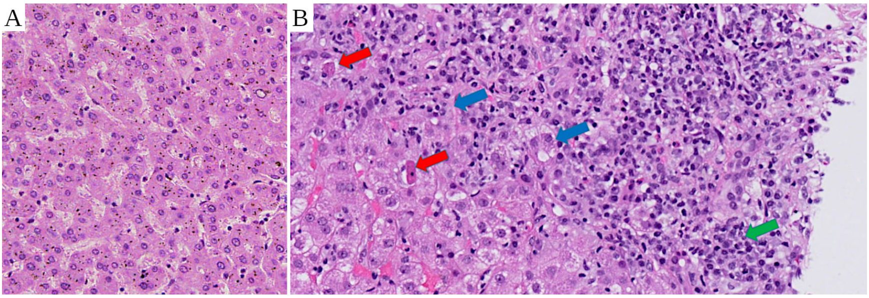



**Figure 4.11** Autoimmune-like hepatitis after mRNA vaccination. **A:** section of normal liver tissue, for reference (adapted from [97]). **B:** vaccine-induced hepatitis. Lymphocytes and plasma cells abound near the top and the right. Red arrows: liver cells undergoing cell death (apoptosis). Green arrow: plasma cell (example). Blue arrows: liver cell rosettes (a morphological marker of inflammation). Image adapted from Vuille-Lessard et al. [157].

within liver cells. Taken together, these findings suggest that liver cells don't express the intact spike protein at high levels, but that the fragments of the expressed amount which is expressed suffice to attract and activate specific CTLs. The key mechanism of vaccine-induced immunological cell and tissue damage by mRNA vaccines put forth by this book is therefore supported by this evidence.

**4.4.7 Clinical case reports on mRNA vaccine-induced hepatitis.** The number of case reports on hepatitis after COVID-19 vaccination is very large; for reviews of such cases, see [158–161]. Many of these reports show histopathological findings, which overall are fairly regular and similar. Infiltrating inflammatory cells include lymphocytes, plasma cells, and sometimes eosinophil granulocytes. The infiltrates are usually concentrated around the branches of the *portal vein*, which drains blood from the intestines toward the liver. A representative example is shown in Figure 4.11.

Most reports chalk up their findings to "autoimmune hepatitis", but in many of these cases there is little or no evidence of autoantibodies, without which this diagnosis is not viable. For example, Izagirre et al. [160] report five cases from a single hospital, but in only one of them did they find any autoantibodies at all. Fimiano et al. [162] report a single case with very high levels of antibodies against SARS-CoV-2, but with no autoantibodies other than against thyroglobulin, a protein found only in the thyroid but not the liver. While their tentative

diagnosis is autoimmune hepatitis, possibly drug-induced, the most likely cause is not autoimmunity but rather immune attack against spike protein expressed by liver cells. We posit that, in the absence of evidence to the contrary, this explanation applies to most other cases of autoantibody-negative hepatitis as well, and probably also to many cases that do show only a narrow spectrum of autoantibodies.

Efe et al. [163] provided an overview of 87 cases of hepatitis after COVID-19 vaccination from multiple clinical centers. Among these, 34 did not exhibit any autoantibodies. The clinical course in these cases was somewhat milder than in those with evidence of autoimmunity, but otherwise the spectrum of clinical and pathological findings was similar. The authors find good response to corticosteroid treatment and good long-term outcomes; this is also the general tenor of the other reports. It bears mention that most of the cases reported by Efe et al. were caused by mRNA vaccines, but 23% were due to the adenovirus-based vaccine produced by AstraZeneca.

Even though the discussion of the pathogenetic mechanism remains vague in general, most reports acknowledge a connection to vaccination, even in those cases that do exhibit autoantibodies. In some cases, causation by the vaccines is supported by recurring attacks of hepatitis after repeated injections; see for example [156, 164, 165]. In summary, therefore, the evidence from the available case reports on vaccine-induced liver disease aligns closely with the expectations which were spelled out above, and which flow from nothing more than the accepted action mechanism of the mRNA vaccines, together with their known strong accumulation in liver cells.

**4.4.8 Kidney disease.** Figure 4.6 illustrated a case of IgA nephropathy, which is one form of *glomerulonephritis*, i.e. inflammation that centers on the kidney glomeruli and is caused by autoimmunity. The second major form of kidney inflammation is interstitial nephritis, of which Tan et al. [166] present one case which occurred after the AstraZeneca adenovirus vaccine, and Mira et al. [167] another one that was observed in connection with the Pfizer vaccine.

Fenoglio et al. [168] reported seventeen cases of biopsy-proven cases of glomerulonephritis, interstitial nephritis, and other forms of nephropathy after COVID-19 vaccination. Thirteen of these occurred in patients who had received an mRNA vaccine. The study also provides references to many other case reports of kidney disease. A series of

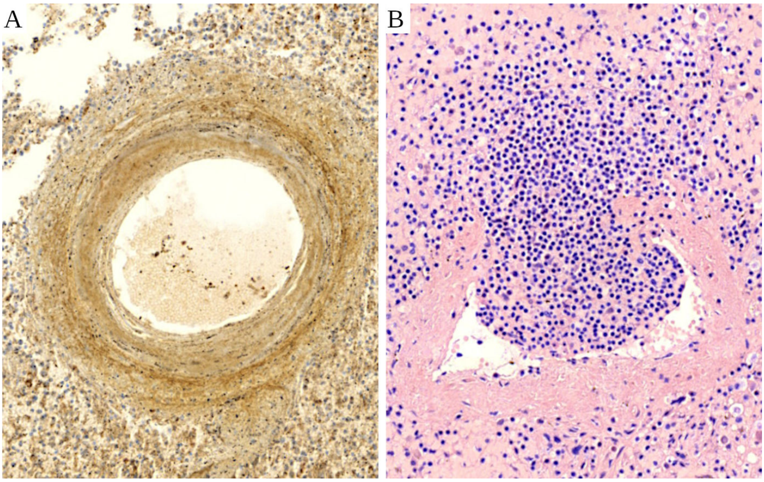



**Figure 4.12** Vaccine-induced vasculitis of the spleen. Cross sections of a spleen artery. **A:** immunohistochemistry for spike protein. Strong expression is observed, with some variation between concentric layers of the vessel wall, which thereby form an "onion skin" pattern. Strong expression is also observed in the surrounding lymphatic tissue. **B:** HE stain. A large lymphocytic infiltrate is seen breaking through the wall of an artery and obstructing the lumen.

six cases from another clinical center was reported by Schaubschlager et al. [169]. Such large case series from individual hospitals suggest that kidney disease after vaccination is not rare.

**4.4.9 Involvement of the spleen.** As of this writing, PubMed finds only one single case report on splenic infarction after vaccination [170], as well as several reports of severe hemolytic anemia or thrombocytopenia which necessitated the removal of the spleen, but no reports on inflammatory disease of the spleen itself. However, Prof. Burkhardt has found several cases with similar and very striking manifestations of vasculitis in the spleen, one of which is illustrated in Figure 4.12. The question therefore arises in how many autopsies of vaccine-related deaths the spleen was even examined in sufficient detail at all.

**4.4.10 Skin manifestations.** Various afflictions of the skin have been reported after injection of COVID-19 mRNA vaccines. A comprehensive review of clinical observations, but without histopathological data, was provided by Kroumpouzos et al. [171]. Studies which include histopathology found several variants of vasculitis [122, 172], but also inflammatory infiltration of the skin's uppermost layer, the *epidermis*,

and of the *dermis*, which is the skin's supporting layer of connective tissue [173–175].

Several reports described cases of *pemphigoid* [171, 176], an autoimmune reaction directed against crucial proteins which fasten the epidermis to the dermis, and whose disruption causes blisters to spring up. Pemphigoid is often triggered by drugs, presumably through the reaction of reactive drug metabolites with the autoantigens in question, as was discussed above in connection with toxic hepatitis (see Section 4.4.4.2).

While most of the reported skin manifestations were transient and not severe, they nevertheless merit diagnostic attention. Biopsies can be obtained from the skin with minimal risk and little effort. Detection in such samples of spike protein expression by immunohistochemistry, and of vasculitis by conventional staining, should influence diagnostic considerations pertaining to any other organs that might be adversely affected by the vaccine. For example, the skin is usually involved in systemic lupus erythematosus (SLE), which has been observed repeatedly after injection of mRNA vaccines and also of adenovirus vector vaccines [177–179]. SLE commonly causes glomerulonephritis but can involve organs other than the kidneys as well.

**4.4.11 Other organs.** Histopathological reports on organs other than those discussed above are comparatively rare. This does not mean that these organs may not be frequently affected; for example, Chee et al. [180] reported twelve cases of Graves disease, an autoimmune affliction of the thyroid, from a single clinic in Singapore; all of these occurred in patients who had received an mRNA vaccine. Similarly, Caron [87] reviewed a sizable number of case reports on thyroid disease.

# 5. Pharmacokinetics and lipid toxicity of mRNA vaccines

In the preceding chapters, we have focused on the immunological mechanisms by which mRNA vaccines induce disease. These mechanisms are essentially the same in different organs; and because the blood vessels are prominently affected, it is clear that disease can strike in any organ. Nevertheless, for a better understanding of vaccine toxicity, it is important to consider where in the body the vaccine particles will accumulate to the highest levels, and for how long they will stay there. Questions of this kind are the subject of *pharmacokinetics*, which we will consider in this chapter. In addition, we will also look at additional mechanisms of mRNA vaccine toxicity, which arise from factors other than the expression of mRNA.

Both the pharmacokinetics of the mRNA vaccines and their chemical toxicity are intimately related to the properties of the lipid nanoparticles. Therefore, this is where we will begin our exploration.

## 5.1 Structure and function of lipid nanoparticles

The composition of an mRNA vaccine lipid nanoparticle is illustrated in Figure 5.1. Such a particle contains four different lipid components, two natural ones (cholesterol and phosphatidylcholine) and two synthetic ones (see Figure 5.2). The least abundant lipid is a synthetic lipid which is coupled to a water-soluble polymer, polyethyleneglycol (PEG), and which decorates the particle surface. The other three lipids are found in the particle interior. Cholesterol and phosphatidylcholine serve to stabilize the particle. The second synthetic lipid is *ionizable*, which means that it can occur in two states of electrical charge. At near neutral pH, which prevails in the extracellular space and in the cytosol, it will mostly be uncharged. On the other hand, inside an acidic environment, these lipid molecules will bind hydrogen ions ($H^+$) and thereby become positively charged. Their mutual electrostatic repulsion

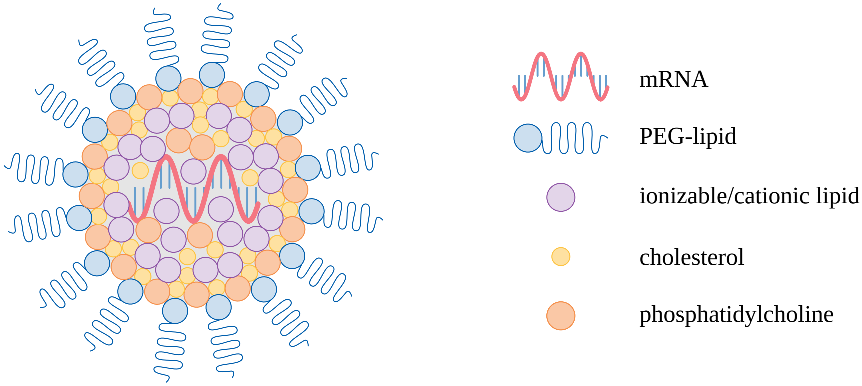



**Figure 5.1** Structure of an mRNA lipid nanoparticle. The surface of the particle is covered with a synthetic lipid that is linked to the hydrophilic (water-soluble) polymer polyethyleneglycol (PEG). The negatively charged mRNA interacts mainly with the second synthetic lipid, which when protonated (i.e. bound to a $H^+$ ion) carries a positive charge. Cholesterol and phosphatidylcholine are naturally occurring lipids that are added for stability.

will cause the lipid nanoparticle to disintegrate and the mRNA to be released into the cell (see later).[1]

**5.1.1 The biomolecular corona.** One important characteristic of the vaccine lipid nanoparticles is the acquisition of a "biomolecular corona", which consists of some of the body's own proteins [181]. The process is facilitated by the PEG-coupled synthetic lipid molecules, which initially cover the surface of the particles. This lipid species is more water-soluble than the others and can detach from the particles, which will expose patches of more *hydrophobic* lipids—i.e., more "greasy" or water-repellent ones. Such a hydrophobic patch will then attract protein molecules which likewise have some hydrophobic surface features (Figure 5.3).

A natural fit for this situation are the *apolipoproteins*. These protein molecules are normally found on the surfaces of the body's own lipid transport particles, the *lipoproteins* (Figure 5.4A). However, other plasma proteins such as albumin, antibodies, and complement factor C3 have also been found on the surfaces of artificial liposomes and lipid nanoparticles [181].

[1] Those molecules of ionizable lipid which interact directly with the negatively charged mRNA inside the lipid particle are most likely positively charged even at neutral pH.

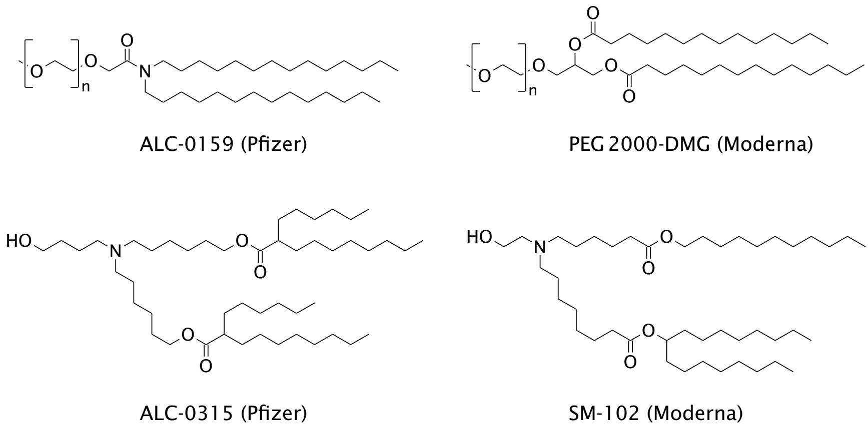



**Figure 5.2** Molecular structures of the synthetic lipids contained in the Pfizer and Moderna COVID-19 vaccines. Each unmarked corner denotes a carbon atom saturated with hydrogen; the large number of such atoms gives these molecules their "greasy" character. Top: the PEG-conjugated lipids. PEG consists of polymeric ethyleneglycol moieties, which are hydrophilic. One such moiety is shown within brackets; the letter n denotes the repetition of approximately 45 such units. Bottom: the cationic lipids. The nitrogen (N) atoms can bind a hydrogen ion ($H^+$) and thereby acquire a positive charge.

The adsorption of apolipoproteins and of plasma proteins to the vaccine lipid nanoparticles is no mere curiosity. The physiological function of the apolipoproteins is to serve as the lipoprotein particles' "address tags"—they direct the transport of lipoproteins into cells and across cellular barriers such as the endothelia of the blood vessels. Accordingly, when the vaccine lipid nanoparticles bind such address tags, they will be recognized and transported much like the body's own natural lipoproteins.

**5.1.2 Receptor-mediated endocytosis and transcytosis of lipoproteins.** The purpose of the natural lipoproteins is to supply the tissues and cells with fat and cholesterol. Cells which require fat or cholesterol will take up those lipoprotein particles by way of *receptor-mediated endocytosis* and then break them down entirely (Figure 5.4B). Fat and cholesterol are used according to the cell's needs; the apolipoproteins are broken down to amino acids, which can be reused for the synthesis of new proteins.

Figure 5.4 also shows that particles that have been taken up by endocytosis may alternatively be released again by *exocytosis*. If endo-

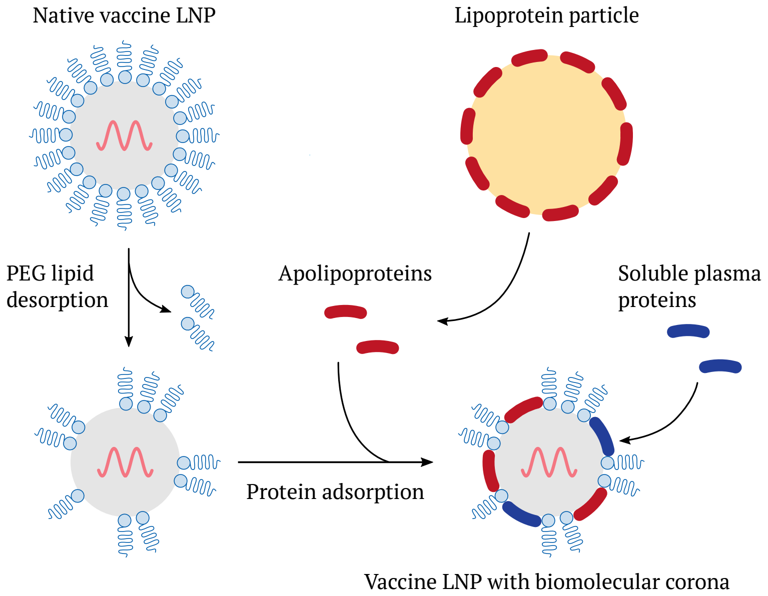



**Figure 5.3** How vaccine lipid nanoparticles acquire their "biomolecular corona." The superficially located PEG lipid can become desorbed from the particles. This exposes other types of lipids, which may then bind various proteins found in the blood plasma. Prominent among these are *apolipoproteins*, which are normally associated with the body's own lipid transport particles, the *lipoproteins*.

cytosis and exocytosis occur on opposite sides of the cell, the effect is *transcytosis*. This is the mechanism by which lipoprotein particles can cross vascular endothelial cells and thereby move between the circulation and the extravascular compartment of our tissues and organs. It appears that this is not limited to the capillaries but can also occur in arteries [182–184].

**5.1.3 Traversal of vascular barriers by lipid nanoparticles.** The same behavior is observed with nanoparticles that carry apolipoproteins on their surface. Kucharz et al. [185] reported that lipid nanoparticles were able to cross the walls of blood vessels in the brain, ending up within the brain tissue.[2] In their study, maximal translocation was detected in *venules*, that is, small veins, rather than capillaries or arteries. Similarly, Hartl et al. [186] reported that polymeric nanoparticles whose surfaces

[2]While Kucharz et al. did not document the role of apolipoproteins, the particles used were of a composition that in vivo would induce the acquisition a biomolecular corona.

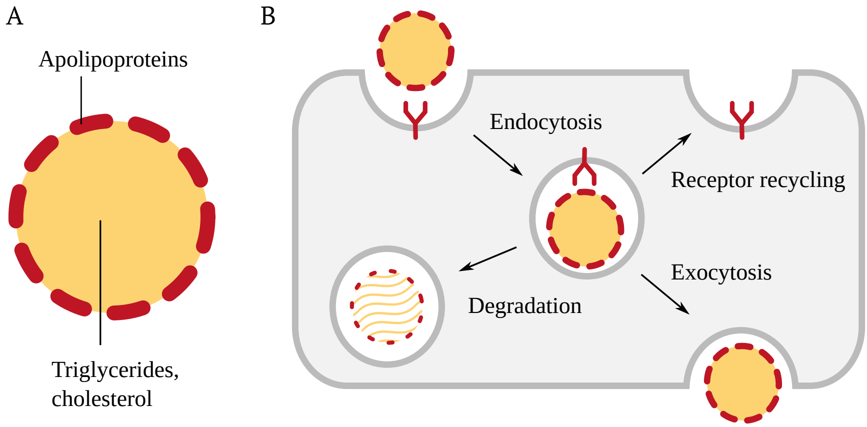



**Figure 5.4** Receptor-mediated endocytosis of lipoproteins. **A:** structure of a lipoprotein particle. The core is a fat droplet which contains triacylglycerol, cholesterol and some other lipids in varying proportion. The surface is decorated with various apolipoproteins. **B:** The apolipoproteins are recognized by receptor molecules on cell surfaces. This recognition will cause the cell to engulf and ingest the particle, which may then be broken down or released again by exocytosis.

had been covalently coupled to one specific apolipoprotein (ApoE) were also able to exit from the circulation into the brain tissue.

Observations such as those reported by Kucharz et al. and Hartl et al. are rather remarkable, considering that the blood vessels of the brain are generally less permissive to solutes and particles than are those of other organs. The anatomical and biochemical features which restrict substance transport from the blood vessels to brain tissue are collectively referred to as the *blood-brain barrier* [187, 188]. The delivery of drugs across the blood-brain barrier is the focus of a disproportionate amount of experimental research on lipid nanoparticle behavior in vivo; transport of such particles into the tissues of other organs receives much less attention. However, without evidence of the opposite, we can assume that transport of such particles across vascular barriers within most other organs of the body will be at least as facile as within the brain. This may very well also include the barrier between the maternal and the fetal circulation within the placenta, but this question has yet to be properly addressed experimentally.

**5.1.4 Intracellular release of the mRNA.** While the biomolecular corona of a vaccine lipid nanoparticle facilitates its receptor-mediated

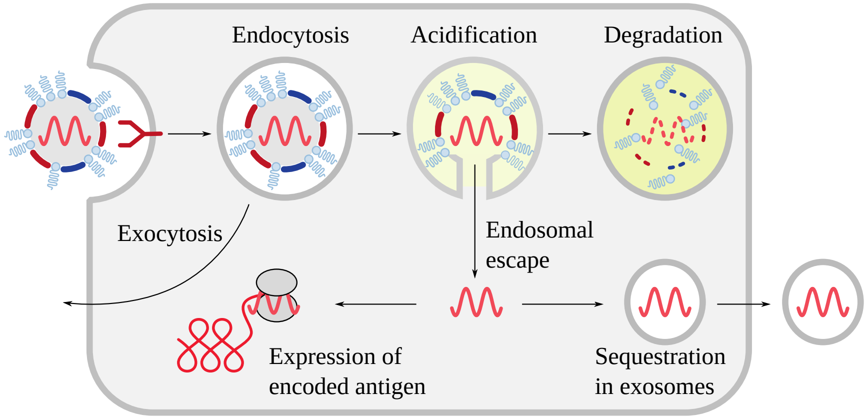



**Figure 5.5** Intracellular fates of mRNA vaccine particles. A vaccine particle that has been taken up by a cell may be released again by exocytosis, or it may remain trapped in the endosome and undergo complete degradation; both processes will compete with the release of intact mRNA from the endosome into the cytosol. mRNA molecules that do escape intact may induce expression of the protein antigen, or they may be packaged into exosomes and released from the cell. Such endosomes may be taken up by other cells, which may then in turn express the antigen.

uptake by a cell, this alone does not guarantee that the mRNA molecules contained within will be successfully released and expressed. Schlich et al. [189] have reviewed several experimental studies which indicate that only a small percentage of all mRNA molecules manage to escape from the endosomal compartment and then be translated into protein. These findings pertain to lipid nanoparticles that were similar in composition but not identical to those used with the COVID-19 mRNA vaccines.

The various alternate fates of the vaccine mRNA are illustrated in Figure 5.5. The escape of the mRNA from the compartment that initially encloses it—the *endosome*—is triggered by *acidification*. The cell pumps acid into the endosome, much in the same way that certain cells within the gastric mucous membrane pump acid into the stomach. The hydrogen ions of the acid then bind to the lipid nanoparticle's ionizable lipid molecules, which will thereby become positively charged. This will cause these lipids to disperse and to mingle with the lipid membrane which encloses the endosome, creating an escape route for the mRNA into the cytosol (Figure 5.6). On the other hand, the acid will

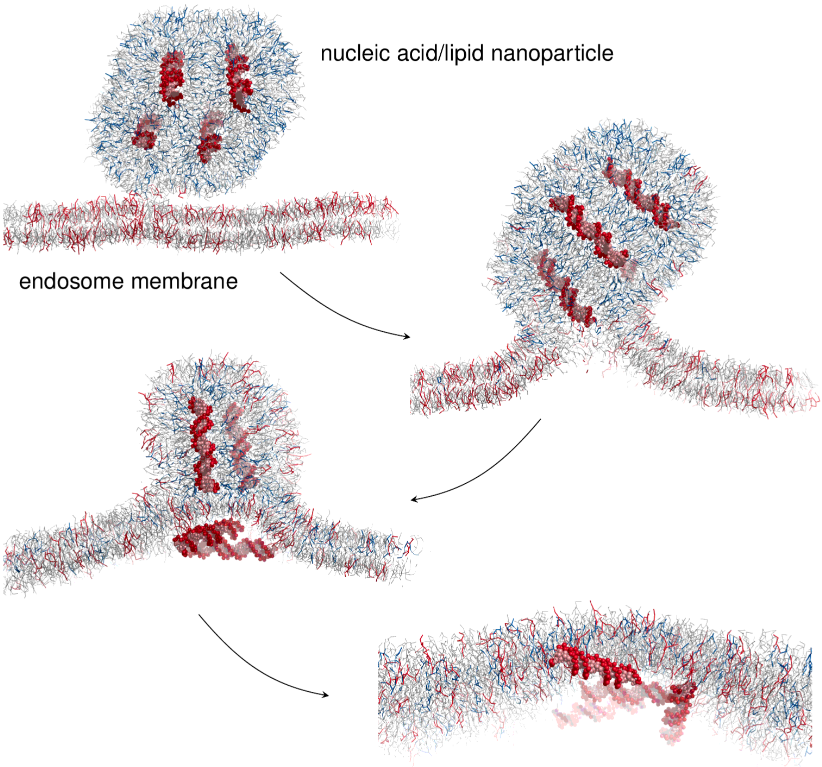



**Figure 5.6** Fusion of a DNA/lipid nanoparticle with the endosome membrane, driven by electrostatic forces between lipid molecules (computer simulation). The positively charged lipids on the LNP (blue) repel each other but are attracted to the negatively charged lipids of the endosome membrane (red). As the LNP merges with the membrane, the helical nucleic acid molecules (red) are released into the cytosol. Rendered with Pymol from coordinates kindly provided by Bart Bruininks [190].

also promote the degradation of both the lipids and the mRNA within the endosome; degradation will compete with release.

Even those mRNA molecules that have managed to escape from the endosome intact may yet be diverted by being packaged into *exosomes*, which may be released from the cell. This might occur before or after the mRNA has been translated within the cell; and furthermore, exosomes may merge with other cells and deliver the mRNA to them. Exosomes may therefore promote the persistence and the spread of the mRNA within the body even after the lipids of the LNPs have been

dispersed, degraded, or excreted; they might well be important in the observed long-lasting expression of spike protein in persons who received COVID-19 mRNA vaccines.[3]

## 5.2 Pharmacokinetics of mRNA vaccines

The properties of the lipid nanoparticles which we considered above exert a strong influence on their transport and their fate within the human body.

**5.2.1 Organ distribution of model mRNA vaccines.** We already noted that the transport of vaccine lipid nanoparticles may resemble that of lipoproteins, which supply our cells with fat and cholesterol. All cells require some cholesterol, and most cell types can burn fat. Nevertheless, the amount of lipoprotein particles taken up and turned over varies greatly between the cells of different organs. The following organs take up particularly large amounts:

1. The liver, which has a central place in lipoprotein metabolism. It synthesizes a large share of all the body's lipoproteins, and it also recycles surplus lipoprotein particles.
2. Endocrine glands that produce steroid hormones. Such glands use cholesterol as a precursor for hormone synthesis. They include the testes, the ovaries, and the adrenal glands.
3. The placenta. It requires lipoprotein both for supplying the fetus and for its own production of progestin hormones, which are necessary to sustain pregnancy.
4. The lactating breast glands. They acquire fat and cholesterol from lipoproteins and repackage them for release into the breast milk.

With this in mind, we can understand some of the observations on the distribution of mRNA vaccines within the body. The data available on this question are rather sparse, but there is one relevant animal study which was performed by Pfizer and submitted to health authorities in

[3]We had noted earlier that the level of protein expression is greatly increased by the replacement of uridine in the mRNA with methylpseudouridine (see Section 2.8.3.2). While this is generally explained in terms of resistance to degradation, the observed kinetics of the expression [56, 57] suggest another explanation, namely, that the methylpseudouridine-modified mRNA escapes more efficiently from the endosomes into the cytosol.

various countries.[4] In this study, rats were injected intramuscularly with a model mRNA vaccine which encoded luciferase, a protein enzyme, rather than the SARS-CoV-2 spike protein. For tracking the movements of this vaccine within the body, the cholesterol contained in the lipid nanoparticles had been made radioactive. The animals were sacrificed at various time points after the injection, and the amount of vaccine in the blood plasma and within different organs was determined by measuring this radioactivity.

Figure 5.7 summarizes the most important findings from this study. As early as fifteen minutes after the injection, the vaccine is detected in the bloodstream. The blood level rises for the first two hours and then drops. Concomitantly, the vaccine accumulates within various organs. We note that in most organs this accumulation reaches its highest level at 48 hours after the injection, which is also the latest data point; we therefore don't know how high it might have risen if measurements had continued for several more days.

Among the organs with the highest tissue levels, we recognize the liver, the adrenal glands, and the ovaries as ones with a high lipoprotein turnover. The testes show a notably lower level of accumulation; one likely reason is that the hormone-producing Leydig cells of the testes account only for a minor fraction of the organ tissue.

On the other hand, the high tissue levels in the spleen are not readily explained by any prominent role of this organ in lipoprotein metabolism. Most likely, elements of the LNP biomolecular corona other than apolipoproteins are responsible for this observation. Spleen tissue is very rich in immune cells, including both macrophages and lymphocytes. Many of these cells possess receptors for antibodies and for proteins of the complement system. These receptors enable the immune cells to ingest antigenic proteins, virus particles or microbial cells to which these antibodies and complement factors have bound. We already noted above that antibodies and complement factors may indeed bind to LNPs, which agrees with this interpretation.

Moderna, according to the EMA's report on this vaccine [58], also submitted some animal data on a model vaccine. This model vaccine contained six different mRNAs, which encoded antigens unrelated to SARS-CoV-2. In this study, the levels of mRNA rather than of the

[4] The Japanese and Australian regulators subsequently released some of these data to the public [191–193]. The FDA and the EMA did not, but from their assessment reports on the Pfizer vaccine [59, 60] it is clear that they, too, had seen the results of this study.

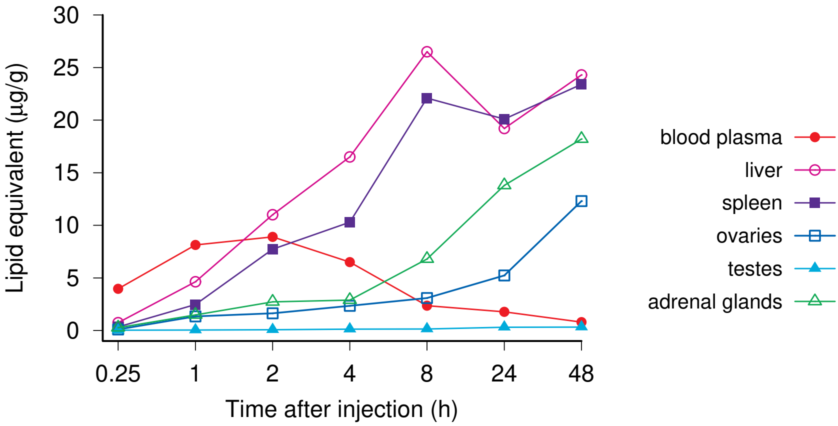



**Figure 5.7** Organ distribution in rats of a model mRNA vaccine with the same lipid composition as the Pfizer/BioNTech vaccine. Plot generated from Table 2.6.5.5B in [191]. The blood plasma level rises soon after injection and then drops as the vaccine accumulates within various organs. The vaccine was measured using a radioactively labeled cholesterol derivative (unlabeled cholesterol is a regular ingredient of the vaccine lipid nanoparticles). The data represent vaccine content in micrograms of vaccine lipid per gram of tissue or milliliter of blood plasma. Note the high concentrations in liver, spleen, adrenal glands, and ovaries.

lipids were measured. The results of Moderna's study are incompletely described in the report, but on page 47 we read:

> *Increased mRNA concentrations (compared to plasma levels) were found in the spleen and eye. . . . Low levels of mRNA could be detected in all examined tissues except the kidney. This included heart, lung, testis and also brain tissues . . . liver distribution of mRNA-1647 is also evident in this study, consistent with the literature reports that liver is a common target organ of LNPs.*

The observed accumulation in spleen and liver agrees with the Pfizer study. While no specific mention is made of ovaries and adrenal glands, the wording suggests that these tissues did not accumulate Moderna's model vaccine to the same degree as Pfizer's.

We note that, regardless of the tissue levels in any specific organ, at least the blood vessels and their endothelia will be exposed to the vaccine particles in each and every organ. Accordingly, vasculitis and thromboembolic events are somewhat likely to occur in all organs.

Additional tissue-specific pathology might be expected to focus on organs with high levels of accumulation. However, as we will see presently, the findings of these animal studies likely do not give a complete picture of mRNA vaccine distribution in practice.

**5.2.2 Correlation of model vaccine organ distribution with histopathological findings.** Among the organs with the highest accumulation of either model mRNA vaccine, only the liver has been extensively studied with histopathological methods; and as we have seen in Section 4.4.7, the literature contains numerous case reports of vaccine-induced hepatitis. Several cases of spleen involvement were reported by Prof. Burkhardt (see Section 4.4.9), but neither ovaries nor adrenal glands appear to have received much scrutiny. Histopathological case reports on the placenta in cases of vaccine-related miscarriage or stillbirth are missing from the literature thus far as well.

On the other hand, we have seen evidence of inflammation and of vaccine-induced spike protein expression in heart muscle (Section 4.4.1) and the brain (Section 4.4.3), even though these organs accumulated only comparatively low or moderate levels of the model vaccine in Pfizer's and Moderna's animal experiments. The observed inflammation is particularly remarkable with respect to the brain, which is supposed to be protected by the blood-brain barrier. In this context, we must note two important caveats:

1. The blood-brain barrier breaks down when the brain tissue is afflicted by inflammation. Accordingly, vasculitis within the brain that was induced by the first injection of an mRNA vaccine might soften up the blood-brain barrier and facilitate the entry of vaccine particles delivered with a subsequent booster injection. It would therefore have been important to examine the organ distribution of the vaccine not only after the first injection, but also after one or more repeat injections. However, this was not done in Pfizer's and Moderna's animal studies.
2. The SARS-CoV-2 spike protein has been shown in several studies to compromise the integrity of the blood-brain barrier [124, 125, 194, 195]. Spike protein which may be expressed elsewhere but reaches the brain through the bloodstream may facilitate penetration of vaccine particles into the brain. In contrast, Pfizer's model vaccine encoded luciferase, which is presumably inert in this regard. Moderna's model vaccine encodes several proteins of Cytomegalovirus;

there seems to be no information on any direct effects of these proteins on blood-brain barrier integrity.

These considerations, in combination with histopathological findings and with the experimental studies discussed in Section 5.1.3 above, strongly suggest that mRNA vaccines distribute more widely and effectively than Pfizer's and Moderna's very limited animal studies on model vaccines would indicate.

**5.2.3 Time course of elimination and duration of activity.** We had seen in Section 5.1.4 that the mRNA can become separated from the lipids after the cellular uptake of the vaccine nanoparticles. The elimination of both ingredients must therefore be considered separately.

**5.2.3.1 Time course of mRNA elimination.** It appears that Pfizer did not provide any data at all on the elimination of the mRNA contained in the company's COVID-19 vaccine, or even on a model mRNA vaccine. The only pertinent data in their animal study [192] consist of measurements of luminescence, which is induced by firefly luciferase, the protein encoded by that model vaccine. Reportedly, luminescence within the liver subsided within two days after injection, whereas the muscle tissue at the injection site showed detectable luminescence for nine days. This suggests, but does not prove that the mRNA itself was inactivated within a similar time frame.

The summary of Moderna's model vaccine study given in the EMA report [58] states that the *half-life* of elimination—that is, the time interval required for the level of the mRNA to drop by half—varied between 15 hours at the injection site and 63 hours in the spleen. It also states that the mixture of model mRNAs was rapidly cleared from the blood plasma, with a half-life of approximately three hours.

While these findings suggest a fairly rapid clearance of the synthetic mRNAs overall, it must be stressed that none of these studies used the mRNA deployed in the COVID-19 vaccines, and furthermore that all studies were carried out in rodents. These results can therefore not be directly applied to the current crop of mRNA vaccines and their use in human patients. As noted in Section 3.2, COVID-19 vaccine mRNA has been detected at 60 days after injection in lymph nodes [66], and at 30 days within muscle tissue of a limb other than the one which had been injected [67]. Long-lasting persistence of the vaccine mRNA in blood plasma samples of injected patients was recently reported by Fertig et al. [196]. According to these authors, all patients still tested positive

on day 15 after the injection, which seems to have been the latest time point to be included. Similarly, Castruita et al. [197] detected vaccine mRNA in blood samples at up to 28 after injection. Collectively, these studies on humans show that the vaccine mRNAs may persist much longer than Pfizer's and Moderna's animal studies would suggest.

**5.2.3.2 Time course of lipid elimination.** The Pfizer vaccine contains two lipids which occur naturally in the human body, as well as two synthetic ones (see Figure 5.2); only the latter will be considered here. According to Pfizer's own data [192], 60% of their proprietary cationic lipid (ALC-0315) will accumulate in the liver after intravenous injection. The level stays remarkably high even at two weeks after the injection, indicating very slow degradation (Figure 5.8). Their PEG-modified lipid (ALC-0159) accumulates within the liver to a lesser degree, which probably reflects its release from the lipid nanoparticles within the circulation, before these particles reach the liver; and this lipid is also more rapidly cleared from the liver tissue.

The report states that both lipids were undetectable in the urine. However, half of the PEG-lipid was excreted in the feces in unchanged form, which is most likely due to its secretion into the bile by the liver cells. In contrast, only 1% of the cationic lipid was found in the feces. Therefore, about half of the PEG-lipid and most of the cationic most likely undergo metabolic degradation. Some lipid metabolites were indeed characterized by in-vitro experiments, but no in vivo studies seem to be available.

According to the EMA report [58], Moderna submitted no data on the elimination of the two synthetic lipids contained in their COVID-19 mRNA vaccine. The EMA report briefly summarizes findings on a "close structural analogue" of SM-102, Moderna's proprietary cationic lipid, stating that no persistence of this analogue beyond one week after the injection was observed in animal experiments. Considering the structural formula of Moderna's PEG-conjugated lipid, fairly rapid degradation appears likely, but no evidence was provided.

While the EMA assures us that accumulation of the lipids within the body is unlikely, we must note that

1. the information provided is entirely insufficient by the usual standards of drug development and approval, and
2. absence of lipid accumulation does not imply absence of cumulative toxicity. This is explained below in Section 5.3.3.2.

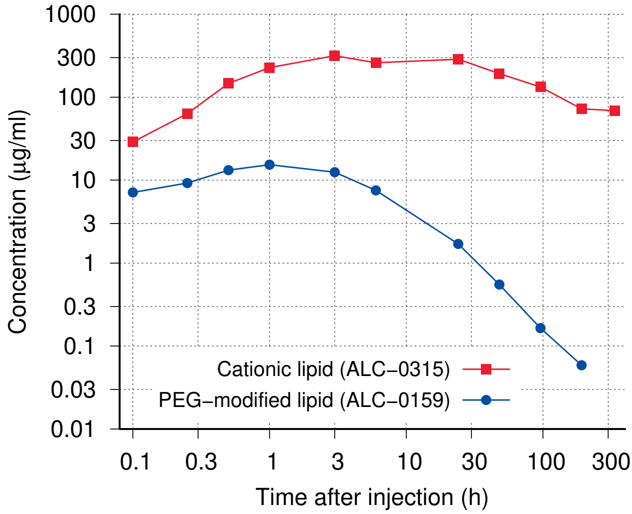



**Figure 5.8** Time course of liver tissue levels of the two synthetic lipids contained in Pfizer's COVID-19 vaccine after intravenous injection. Data from [192]. Note that both the $x$-axis and the $y$-axis are logarithmic.

**5.2.4 Accidental intravascular injection.** In Section 5.2.3.2, we saw that in experimental animals injected intravenously a very large proportion of the vaccine ends up in the liver. Presumably, other interior organs, too, will receive higher amounts of vaccine after intravenous than after intramuscular injection.

Human patients receive the COVID-19 vaccines intramuscularly, and if the injection works as intended, then much of the injected substance will indeed be retained in the muscle tissue, at least initially. However, as any nurse or physician will know, even with careful technique of intramuscular injection—i.e. with prior aspiration [198–200]—the bolus will sometimes accidentally be delivered directly into the bloodstream. Middleton et al. [201] found that partial or complete injection into the bloodstream occurred in 1.5-2% out of more than 3000 injections of testosterone. The rate may be similar with the COVID-19 vaccines—or even higher, considering that these were sometimes administered by auxiliary personnel with little training. In such cases, a large fraction or even all of the injected vaccine will be systemically distributed.

Animal studies have shown, unsurprisingly, that myocarditis caused by mRNA vaccines is more severe after intravenous than after intramuscular injection [202]. The same must be assumed to be the case

with humans and with damage to other organs. It is quite possible that many of the most severe and acute adverse vaccine effects were related to such accidental intravenous injection.

## 5.3 Lipid nanoparticle toxicity

We will again limit this discussion to the two synthetic lipid species. The PEG-conjugated lipids are the less abundant of the two, and the only mechanism of harm on record consists in allergic reactions to these lipids. In contrast, the cationic lipids account for almost half of the total lipid in the vaccine LNPs, and they can exert toxicity outright, without any "help" from the adaptive immune system.

**5.3.1 Allergic reactions caused by PEG-conjugated lipids.** Polyethyleneglycol (PEG)-conjugated lipids are not known to cause significant toxicity through chemical reactivity or physical disruption of cellular structures. However, they may trigger allergic reactions in those individuals whose blood plasma contains antibodies against PEG. Such antibodies may have arisen in response to the initial injection with an mRNA vaccine, and the allergy might then become clinically manifest after a subsequent injection with the same or another mRNA vaccine. However, antibodies to PEG have also been found in blood samples of patients who had never received any injections with an mRNA vaccine, nor with any other PEG-containing medicine [203]. In such patients, the antibodies may have been induced by laxatives or cosmetics containing PEG, but immunological cross-reaction with other chemicals also seems possible.

PEG allergy manifests itself clinically as *anaphylaxis*, i.e. it sets in shortly and acutely after the injection. It induces welts on the skin, and in some patients also anaphylactic shock [204], i.e. circulatory failure. This is analogous to bee or wasp sting allergy, which is most dangerous if the poison is perchance delivered directly into the bloodstream. Anaphylactic shock in response to an mRNA vaccine may well involve accidental intravenous injection, too.

Anaphylaxis is caused by the release of specific inflammatory mediators—histamine, platelet-aggregating factor, and leukotrienes—from inflammatory cells, particularly *mast cells*. The most straightforward trigger for this release is antigen-specific immunoglobulin E (IgE). However, other mechanisms can contribute, in particular complement activation, which may be induced by the more common and abundant IgG

and IgM antibodies. IgG an IgM against PEG have been documented in clinical cases of PEG allergy [205]. Whether or not PEG-specific IgE also occurs in such cases has apparently not yet been determined.

The binding of antibodies to PEG-conjugated medicines and the subsequent activation of complement will also accelerate the removal of these medicines from the circulation by phagocytes [206]. In the case of the mRNA vaccines, such accelerated clearance might modify the immune response to the encoded antigen.

**5.3.2 Inflammatory signaling by cationic lipids.** Several experimental studies have shown that cationic lipids similar to those used in the Pfizer and Moderna COVID-19 vaccines induce strong inflammatory reactions. The spectrum of cellular signaling pathways involved is rather broad and somewhat variable between different lipid species Lonez et al. [207]. A recent study by Ndeupen et al. [85] demonstrated strong inflammatory responses to synthetic lipid nanoparticles with or without RNA. The cationic lipid used in this study was proprietary, and its chemical structure was not specified, but it was most likely similar to the two cationic lipids used in the COVID-19 vaccines (see Figure 5.2). This agrees with the frequent observation of local and also systemic inflammatory reactions among COVID-19 vaccine recipients; however, from such clinical observations alone it is not possible to discern the respective contributions of mRNA and of lipids to the inflammation.

We had seen in Section 2.2.2 that the induction of a specific immune response requires the activation of non-specific defense mechanisms, which may come about either by outright tissue damage or by the stimulation of various pattern recognition receptors. The protein antigens contained in conventional vaccines will not usually themselves provide either kind of stimulus. Such vaccines are therefore supplemented with so-called *adjuvants*, that is, natural or synthetic substances which provide the missing non-specific immune activation. In keeping with their proinflammatory effect, cationic lipids have been shown to act as adjuvants [208, 209]. It is likely that the cationic lipids contained in the COVID-19 mRNA vaccines also function in this manner, in addition to their essential role in the intracellular release of the mRNA.

**5.3.3 Chemical toxicity of cationic lipids.** The ability of cationic lipids to release the vaccine mRNA from the endosomal compartment depends crucially on their positive charge. The natural lipids which form the cell's membranes are all either neutral or negatively charged (anionic).

Cationic molecules of different kinds will be strongly attracted to these negatively charged cell membranes, and they will tend to destabilize and disrupt them (cf. Figure 5.6). There are many variations on this theme. For example:

- our own phagocytes produce cationic peptides, which they use to disrupt the cell membranes of pathogenic microbes [210];
- proteins may contain positively charged peptide motifs that facilitate their translocation across membranes [211]; and
- cationic detergents disrupt the cell membranes of microbes and tend to be effective disinfectants [212].

The ionizable lipids such as those used in the current COVID-19 vaccines will only be partially charged at the concentration of $H^+$ ions (or the pH value) that prevails within the cytosol, i.e. within the cell at large, outside the endosome. This is an improvement over previous generations of cationic lipids that will carry a positive charge at all times, regardless of pH. Nevertheless, even these ionizable lipids will remain charged within the cytosol to some degree, and therefore able to disrupt cell membranes.

**5.3.3.1 Cationic lipids induce reactive oxygen species.** A key effect that occurs downstream of the membrane disruption by cationic lipids is the production of *reactive oxygen species* (ROS). There are several membrane-associated enzyme systems likely to be involved in producing these ROS, including NADPH oxidase and the mitochondrial electron transport chain [213]. Regardless of the exact mechanism of their generation, these ROS will attack various sensitive targets within the cell, including both membrane lipids and DNA [214]. Membrane damage to the mitochondria is likely to amplify the production of ROS. Damage to mitochondria or to the cell's DNA will trigger apoptosis.

In this connection, we must note that of all cell types in the body the lymphocytes are far and away the most susceptible to apoptotic stimuli.[5] While Filion and Phillips [216] found macrophages to be more susceptible to the cytotoxic effects of a cationic lipid, it must be noted that they employed a rather different lipid mixture, and the susceptibility profile might be different with the lipids contained in the COVID-19 vaccines. Immunohistochemistry has shown COVID-19

[5] See in particular the example of adenosine deaminase deficiency, a metabolic disease that causes genotoxic stress to all body cells yet selectively eradicates the lymphocytes. This causes severe combined immunodeficiency (SCID) [215].

mRNA vaccines to induce expression of spike protein in lymphocytes, which suggests that these may be subject to chemical toxicity from the lipid nanoparticles as well. Since the lymphocytes are the backbone of the adaptive immune system, we must expect that cationic lipid toxicity will cause immunosuppression.

Reactive oxygen species also arise within normal cell metabolism, and accordingly our body cells have some capacity to scavenge them and to mitigate the damage. An important scavenger for ROS and their various toxic conversion products is the thiol compound glutathione (G – SH). It is noteworthy that cellular glutathione levels vary greatly between different tissues; for example, Hazelton and Lang [217] reported that in rats G – SH levels were three times higher in the kidney than in the heart, and three times higher again in the liver. Thus, while the liver tends to strongly accumulate lipid nanoparticles, it also has the largest metabolic reserve for coping with lipid toxicity. Other organs with lower G – SH reserve might suffer more severe damage than the liver in spite of lower LNP tissue levels. This is one of the many questions that should have been, but were not addressed in preclinical safety testing of the COVID-19 vaccines.

**5.3.3.2 DNA damage is cumulative.** Broadly speaking, drug effects may be reversible or irreversible. Alcohol is a good example of a drug that can have both reversible and irreversible effects: the effect of alcohol on mood and vigilance subsides when it is inactivated by metabolism, whereas alcohol-induced inflammation of the liver will fester and may turn into cirrhosis, which is permanent even after complete withdrawal of the drug.

Reversible drug effects will give rise to cumulative toxicity only if the drug itself accumulates within the body, that is, if repeated applications occur before previous doses have been completely eliminated. However, as the example of liver cirrhosis illustrates, the same is not true of irreversible drug effects. DNA damage is by its very nature irreversible, even though some DNA lesions are successfully reverted by the cell's DNA repair systems. Since ROS induced by cationic lipids induce such DNA damage, we must assume that these lipids pose a problem of cumulative toxicity regardless of their own accumulation as such.

**5.3.3.3 Toxicity of experimental or approved LNP drugs and vaccines.** The most favorable reports on the toxicity of any LNP-based drug concern the single such drug that has passed a regular approval process.

The RNA contained in this drug (patisiran, Onpattro®) is not an mRNA—it is designed not to induce the expression of a foreign antigen, but rather to reduce ("silence") the expression of a "self" protein. This protein, *transthyretrin*, is produced in the liver, and accordingly the lipid nanoparticles contained in patisiran have been optimized for accumulation in this organ.[6]

The composition of the LNPs employed in this drug is rather similar to those used in Moderna's and Pfizer's COVID-19 vaccines. Here, one must note that patisiran is applied at far higher doses than are the COVID-19 vaccines; the uniformly favorable reviews on its safety [218–220] are therefore quite remarkable. Considering this ostensibly positive experience, we might ask why the same lipid nanoparticle system was not used by Moderna in their attempts to treat another metabolic disease concerning the liver, namely, Crigler Najjar syndrome. While "proof of concept" studies on this treatment in animals have been presented [221], insurmountable toxicity problems reportedly were the reason behind the company's decision to abandon this effort and turn to vaccines instead [222, 223].

Preclinical data on the toxicity of the cationic lipids contained in Pfizer's and Moderna's COVID-19 vaccines are too sparse to permit any definitive conclusions as to their degree of toxicity in humans. However, some results which are briefly summarized in the EMA report on the Moderna vaccine, and which point to measurable levels of DNA damage, will be discussed in Chapter 6.

## 5.4 Appendix: Evidence of substandard manufacturing Quality of COVID-19 mRNA vaccines

In studying the interactions of a drug or vaccine with the human body, an implicit assumption is that the quality of the product is very consistent, so that data acquired with different production lots are indeed comparable. However, the evidence shows that with the COVID-19 mRNA vaccines this assumption breaks down.

[6] Transthyretrin circulates in the blood plasma and transports the major thyroid gland hormone (thyroxine, $T_4$). In some rare patients, aberrantly folded transthyretrin molecules may form deposits ("amyloid"), which can damage the function of the heart and the peripheral nerves. Reducing the expression of the protein using patisiran reportedly improves clinical outcomes [218].

**5.4.1 Contaminants detected in mRNA vaccines.** At least two kinds of contaminations have been clearly documented, namely, metallic particles and plasmid DNA.

**5.4.1.1 Metallic particles.** A thorough microscopic and spectroscopic investigation by a group of senior academics has provided clear evidence of metallic particles in both Pfizer's and Moderna's mRNA vaccines. These are comprised of transition metals (cobalt, iron, chromium, and titanium), as well as rare earth metals (cerium and gadolinium) and various other elements [224]. The size of these particles varies from 1 µm to 0.1 mm, which means that some of them are large enough to be visible to the naked eye.

The particles might constitute abrasive debris from pumps and valves in the equipment used in the production of these vaccines. Normally such debris is removed from pharmaceutical products by a final filtration step. Their occurrence in the final product in the vaccines indicates that corners were cut in production. The possible health effects of these contaminants remain to be elucidated.

**5.4.1.2 Plasmid DNA.** The mRNA contained in the vaccines is made using a DNA template, which is part of a so-called *plasmid*, i.e. a DNA molecule which is able to replicate inside bacterial cells. This template DNA should be completely removed from the reaction mixture before the mRNA is combined with lipids into mRNA/lipid nanoparticles. However, it seems that again corners were cut, causing at least some vaccine batches to be contaminated with astonishingly high amounts of plasmid DNA [225]. The possible consequences are discussed in Section 6.3.

**5.4.1.3 Other contaminants.** The presence of other contaminants in the vaccines has been alleged, in particular of graphene or graphene oxide. However, we have not seen robust experimental evidence of this.

**5.4.1.4 Lipid impurities.** We noted above that the mRNA vaccine nanoparticles contain two unnatural lipid species, which are crucial for their uptake into our body cells (see Section 5.1). While the two manufacturers employed somewhat different synthetic lipids, all of these lipids have one thing in common: they contain unknown amounts of unknown impurities. In its assessment report on the Pfizer vaccine, the European Medicines Agency (EMA) notes, with respect to Pfizer's cationic lipid ALC-0315 [60, p. 24]:

> *Lipid-related impurities have been observed in some recently manufactured finished product batches, correlated with ALC-0315 lipid batches. The quality of ALC-0315 excipient is considered acceptable based on the available data on condition that specific impurities in the finished product will be further evaluated.*

Similarly, the EMA report on the Moderna vaccine observes [58, p. 23]:

> *Numerical limits for specified and unspecified impurities will be included in the PEG2000-DMG specification post-approval. The current reporting of impurities is not acceptable. Characterisation data for impurities which are reported under 'content of unknown' should be provided post-approval.*

With respect to Moderna's cationic lipid SM-102, the same report comments:

> *CQAs [critical quality attributes], CPPs [control process parameters] and critical attributes of the materials used for the manufacture of SM-102 are missing.*

It is quite astonishing that EMA and other regulators granted approval "proactively" even before the nature and the amounts of such lipid impurities had been accurately determined.

**5.4.1.5 Implications.** We must note that all known contaminants were found by researchers without affiliation to the manufacturers or the regulators. The conclusion is unavoidable that both manufacturers and regulators have acted with gross negligence. This inference is reinforced by the reckless manner in which EMA and other regulators brushed aside concerns over lacking quality information pertaining to the novel lipids used by both manufacturers and proceeded with approval.

**5.4.2 Batch-to-batch variability of adverse event reports.** Aside from the detection of contaminations, a second line of evidence to prove the inconsistent manufacturing standards of the COVID-19 mRNA vaccines is the large variation in the number of reported adverse events between production batches. This is clearly illustrated for the Pfizer vaccine in Figure 5.9A, which shows adverse event reports from Denmark, mostly from the year 2021 [226]. The batches can be separated into three clusters with very high, intermediate, and low adverse event incidence, respectively.

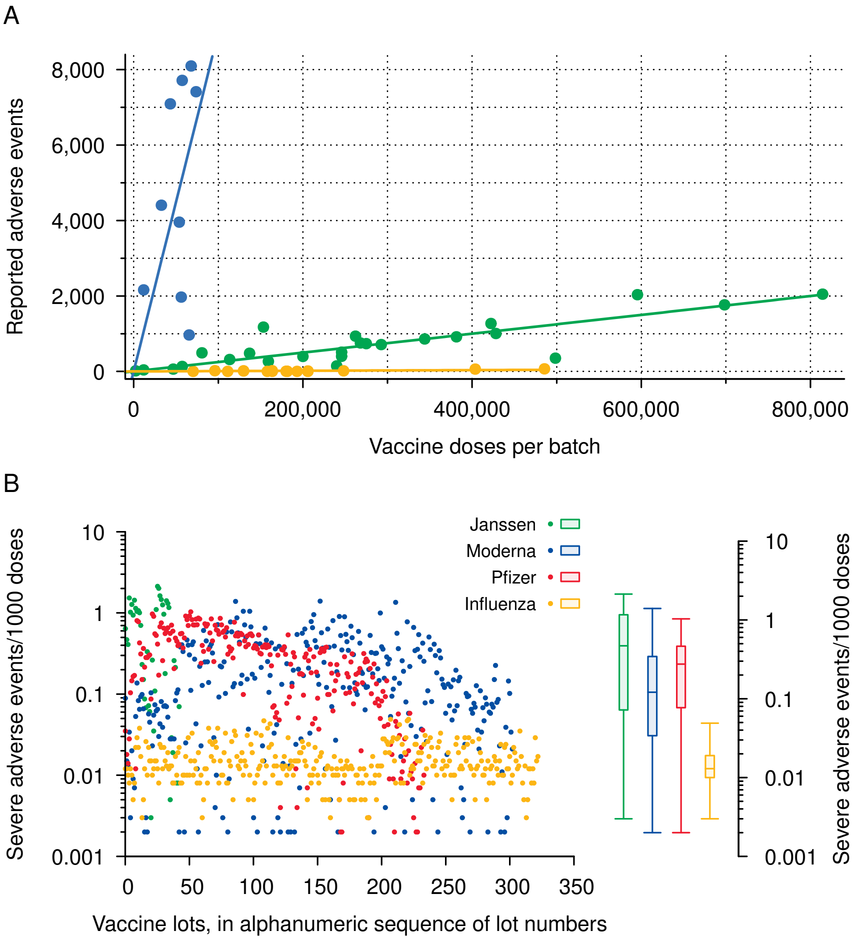



**Figure 5.9** Batch-to-batch variability of adverse event incidence. **A:** Batch-dependent variation in the number of reported adverse events after Pfizer-BioNTech mRNA vaccination. Dispensed doses and adverse event reports pertain to Denmark only. Reporting period: December 27, 2020 to January 11, 2022. Each dot represents a single vaccine batch. The batches fall into three separate clusters, which are identified using different colors and separate linear regression lines. Replot of Figure 1 in Schmeling et al. [226]. **B:** Severe adverse events reported to VAERS, by batch, for three different COVID-19 vaccines and several brands of influenza vaccines. The data comprise a total of approximately 600 COVID-19 vaccine batches as well 323 influenza vaccine batches; the reports for the latter were filed in 2019. Note the logarithmic $y$-axis. In the box plots, the box for each type of vaccine shows the median and the upper and lower quartiles, with whiskers spanning the entire data range. Based on work by Sasha Latypova, Craig Paardekooper, and Jason Morphett.

The large variation between batches in the number of adverse event reports is also evident from data in the VAERS system, and for all three gene-based COVID-19 vaccines that have been used in the United States. Figure 5.9B compares the incidence of severe adverse event reports per batch of these vaccines to those of influenza vaccines. With each of the three COVID-19 vaccines, the incidence is not only much higher on average, but also much more variable than with the influenza vaccines. This high variability shows that the product quality is quite inconsistent between batches.

# 6. Genotoxicity of mRNA vaccines

Genotoxicity means toxic damage to our genes, that is, to our DNA. It may affect the *germline cells*, which include the oocytes in the ovaries and the sperm-producing cells in the testes, or the *somatic* cells, which comprise all cells of the body which are not part of the germline. Genotoxicity is sometimes used for therapeutic purposes. The effects of ionizing radiation and of cytotoxic anticancer drugs such as cyclophosphamide or cisplatin are almost entirely due to DNA damage. The purpose of such treatment is to drive cancer cells into apoptosis. It is of course fraught with side effects: apoptosis will not be limited to cancer cells alone, but also affect healthy cells e.g. in the bone marrow and the hair follicles, leading to a drop of all kinds of blood cells and to hair loss. Induction of mutations in surviving cancer cells may in the long term enhance the growth of the cancer, and mutations in previously healthy cells may induce new, secondary malignancies. At lower intensity, DNA damage will not trigger outright cell death, and therefore no acute clinical symptoms; nevertheless, the risk of mutations and therefore of inducing cancer still applies.

The mRNA vaccines may, subsequent to their cellular uptake, give rise to genotoxicity along three distinct pathways:

1. the cationic lipids contained in the lipid nanoparticles can induce the formation of reactive oxygen species (ROS), which may react with DNA;
2. the mRNA itself may undergo reverse transcription into DNA, which will then insert into the chromosomal DNA. This may result in the disruption or dysregulation of cellular genes;
3. DNA which is present as a contamination in the mRNA vaccines may insert into our chromosomal DNA, too.

While the first two mechanism are inherent in the technology and according to the current state of knowledge must be considered un-

avoidable, the third one should be avoidable in principle. However, recent data show that high levels of contaminating DNA are present at least in certain production batches of both Pfizer's and Moderna's mRNA vaccines (see Section 6.3).

## 6.1 Genotoxicity of synthetic cationic lipids

We had discussed in Section 5.3.3 that cationic lipids may induce reactive oxygen species (ROS), which in turn may cause DNA damage. We might ask if there is a threshold value below which the use of such agents would be perfectly safe. We have no direct evidence to answer this question. However, the example of ionizing radiation, whose effects are likewise mediated by ROS, suggests that there is no safe threshold. Prenatal exposure to even the low doses of radiation which are used in X-ray diagnostics will cause a measurable increase in the incidence of childhood cancer and leukemia. First reported in 1956 by Stewart et al. [227],[1] this finding initially met with widespread skepticism, but it was later confirmed in two independent large-scale studies in the UK [228] and the U.S. [229]. While the risk's exact magnitude remains under debate, it is generally considered similarly high as in the first decade after birth, which is the most sensitive period of extra-uterine life [230]. Even though the dose-adjusted cancer risk of ionizing radiation declines with increasing age, it will not drop to zero. The same must be expected with DNA damage caused by chemical agents, including cationic lipids.

But is there any actual evidence of DNA damage from the lipids contained in the COVID-19 mRNA vaccines? According to the EMA assessment report on the Pfizer/BioNTech vaccine [60], this manufacturer did not provide any experimental data on the potential cytotoxicity of their lipid mixture (and the EMA committed a grave mistake in letting them get away with it). In contrast, Moderna, in its own application to the EMA, did supply some data from animal experiments. These data pertained to erythrocytes (red blood cells, RBC) which were *polychromatic* and to those with *micronuclei.*

**6.1.1 Increased abundance of polychromatic red blood cells.** Polychromatic RBC are those which have only just finished their differentiation inside the bone marrow and, as the final step of that maturation,

[1] The X-ray doses used in diagnostic imaging at the time were considerably higher than those in use today, yet nevertheless far lower than those required then and now in therapeutic irradiation.

have expelled their cell nuclei. At this stage, they still retain their ribosomal RNA within the cytosol, which causes them to appear bluish rather than red in the Giemsa stain; the latter is a routine method used for differentiating cell types in blood smears.

Changes in the percentage of RBC which are polychromatic indicate changes in erythrocyte maturation kinetics. Genotoxic agents may either decrease [231] or increase [232] this parameter. In animals exposed to a model vaccine that contained SM-102, the company's proprietary cationic lipid, Moderna found a significantly decreased level of polychromatic RBC [58, p. 50]. However, this effect was observed only in male rats. This unexpected gender difference casts doubt on the statistical power of Moderna's study.

**6.1.2 Increased abundance of micronuclei.** Using a different model mRNA but again the same lipid mixture that includes SM-102, Moderna found [58, p. 50]

> *statistically significant increases in micronucleated erythrocytes ... in both sexes.*

A so-called micronucleus is a chromosome fragment which arose through chromosome damage within an RBC precursor cell, and which was then left behind in the cytoplasm when the main nucleus was expelled [232, 233]. Counting RBCs with micronuclei is a straightforward and widely used test for the detection of genotoxicity in vivo [233].

The EMA report on the Moderna vaccine cites a study submitted by the company which proposes that the observed increase of micronucleated RBC might have been due not to genotoxicity, but rather to the impeded clearance of these cells from the bloodstream. This impeded clearance in turn is blamed on the vaccine's toxicity to the spleen, the organ which is responsible for breaking down damaged or expired red blood cells. However, no proof of this rather brazen contention is shown; and the EMA report further states that

> *a strong increase in molecular initiating events ... was observed 48 hours after the final administration in the highest dose group in male rats.*

While no details are given as to the exact nature of the event which was observed, the phrase "increase in molecular initiating events" clearly suggests an actual rise in the rate of formation of genetically damaged cells, rather than merely a decrease in their clearance.

**6.1.3 Conclusion.** While the available description of Moderna's experimental findings is rather incomplete, it strongly suggests that the SM-102 lipid contained in the company's COVID-19 vaccine indeed causes DNA damage. This agrees with prior observations of genotoxicity associated with liposomes containing similar cationic lipids, reviewed for example by Inglut et al. [234]. Unless proof positive to the opposite is provided, we must assume the same with Pfizer's structurally similar ALC-0315 lipid.

We stress again that any form of genotoxicity, at any dose, implies a certain risk of cancer and leukemia. Thus, the prospect of frequently repeated COVID "booster shots," as well as of extending mRNA technology to vaccines against other pathogens or non-infectious diseases, conjures up a significant public health risk.

## 6.2 Reverse transcription of vaccine mRNA sequences into DNA

The second major risk of genotoxicity posed by mRNA vaccines arises from the mRNA component itself. In connection with the emergency use authorizations for the COVID-19 mRNA vaccines, this risk was altogether disregarded by the EMA and other regulators. It will, however, become clear in the following that this cavalier approach was scientifically unjustified.

**6.2.1 The genotoxicity risks of recombinant RNA were dismissed based on outdated science.** In the EMA assessment report on the Pfizer vaccine, we find the following succinct statement [60, p. 50]:

> *No genotoxicity studies have been provided. This is acceptable as the components of the vaccine formulation are lipids and RNA that are not expected to have genotoxic potential.*

Apparently, EMA's experts were under the impression that RNA in general will not affect the integrity of the host cell genome. The first exception to this rule has been known since 1970, when oncogenic retroviruses were found to carry a *reverse transcriptase* activity. This enzyme will copy the viral RNA genome into DNA, which then inserts into the host cell genome [235, 236]. The realization that eukaryotic cells themselves have similar reverse transcriptase activities came several years later [237], but it could hardly be considered a novelty in 2020.

**6.2.2 Genomic insertion of RNA viruses through cellular reverse transcriptase activities.** The first studies to demonstrate the chromosomal insertion of mammalian DNA sequences that were derived from an RNA virus which was *not* a retrovirus were reported by Klenerman et al. [238] in 1997. The virus in question was Lymphocytic Choriomeningitis Virus, which infects mice. Since this virus does not itself encode a reverse transcriptase enzyme, it followed that the observed partial DNA copies of the viral RNA genome had to have been created through reverse transcription by cellular enzymes. The molecular mechanism was later elucidated in detail by scientists from the same laboratory [239]. It turned out that a *retrotransposon* had accomplished both the reverse transcription of the viral RNA and the insertion of the DNA copy into the cellular genome.

**6.2.3 The biological role of cellular retrotransposons.** Retrotransposons are mobile genetic elements in the cellular genome that encode the complete protein apparatus for generating additional copies of themselves. Most of the time, it is the mRNA of the retrotransposon itself that ends up being copied back into DNA and inserted. However, the retrotransposon proteins may occasionally undergo a *template switch*—they may lose their own mRNA template and pick up another RNA molecule instead, which will then undergo reverse transcription into DNA and be inserted into the cellular genome (Figure 6.1).

There are several homologous families of retrotransposons, of which in humans the most active and important one is the LINE-1 family [240–242]. Since the location of new insertions within the genome is largely random [243], the biological outcomes are quite varied. If the insertion occurs within a functional gene, that gene may be disrupted; if insertion occurs in the vicinity of a functional gene, then the activity of the latter may be regulated upward or downward (see Section 6.4.2). Depending on the specific role of the affected gene, the behaviour of the cell may be changed, and cancer or other diseases may result [244, 245].

While their activity varies between the types and functional states of our body cells, it is noteworthy that retrotransposons are active in both dividing and non-dividing cells [246] and also in oocytes [247]. We must therefore expect that viral or other foreign RNAs may be inserted by retrotransposons into the genomes not only of somatic cells, and thereby potentially cause cancer, but also of germline cells, and therefore propagate within the human population.

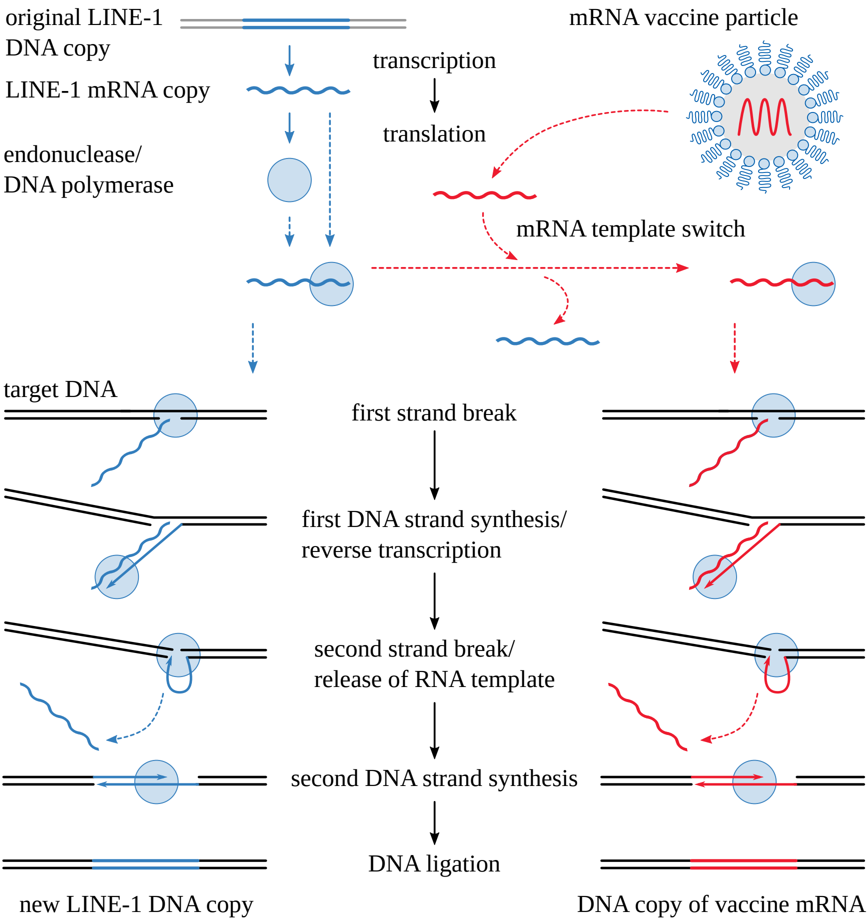



**Figure 6.1** How the LINE-1 retrotransposon may copy a vaccine mRNA into DNA and insert it into the host cell genome. The process begins with the transcription of an existing LINE-1 instance into an mRNA copy. Translation of this mRNA produces two proteins, one of which is a bifunctional endonuclease/DNA polymerase, i.e. it can both cut DNA and synthesize it. This molecule binds to the LINE-1 mRNA and then finds a new DNA target site. It cleaves the first DNA strand. Through reverse transcription, it then extends one of the free ends with a DNA copy of the mRNA. Once this step is complete, the second strand of the target DNA is cleaved, and the second strand of the new LINE-1 copy is synthesized along the first. The process can be usurped early on by another mRNA molecule, such as a vaccine mRNA, which dislodges the LINE-1 mRNA from its endonuclease/polymerase. Such a template switch will produce an inserted DNA copy of the substitute RNA.

**6.2.4 Genomic DNA sequences derived from non-retroviral RNA viruses.** A multitude of RNA viruses other than retroviruses have given rise to partial DNA copies found in the genomes of mammals and other vertebrates [248–251]. Similar findings have been made in other eukaryotic organisms such as fungi, plants and protozoa [252–254]. All of these virus-derived sequences must have arisen through some kind of retrotransposition mechanism, which clearly substantiates the above point that retrotransposition can occur in the germline cells of all these species.

While all observations cited here pertain to sequences derived from RNA viruses, retrotransposition by LINE-1 is not sequence-specific [255], and there never was any reason to exclude the possibility that other RNA sequences, such as for example those of the Pfizer or Moderna mRNA vaccines, would be subject to the same mechanism.

**6.2.5 Genomic insertion of SARS-CoV-2 sequences in infected cells.** Already in 2021, it was demonstrated that partial DNA copies of the genomic RNA of the SARS-CoV-2 virus can insert into the cellular DNA of infected cells, both in cell culture and in patients infected with the virus [256]. Even though this does not directly relate to the mRNA vaccines, it does show that SARS-CoV-2-derived RNA sequences are not exempt from the general mechanism. Moreover, this study demonstrated that the insertion was mediated by LINE-1 retrotransposons.

**6.2.6 Detection of spike gene DNA copies in vaccine-exposed cells.** Of even greater and more immediate relevance is the recent study by Aldén et al. [257] on a human-derived liver cell line, which they exposed to the Pfizer vaccine. The authors detected DNA copies of the spike protein gene within those cells (see Figure 6.2), which they took as evidence of reverse transcription. The findings reported in this initial study suggest but do not rigorously prove the participation of LINE-1 in this apparent retrotransposition event. However, all of the active retrotransposons within the human genome belong to the so-called *non-LTR* class [258], with which the reverse transcription of the RNA into DNA is inextricably linked to its insertion into the DNA, as is illustrated for LINE-1 in Figure 6.1. Thus, while we can't be absolutely certain that DNA copy of the vaccine sequence was indeed generated by LINE-1, this question is not crucial—if we accept the DNA copies were generated by reverse transcription, then we must also assume that they became concomitantly inserted into the cellular genome.

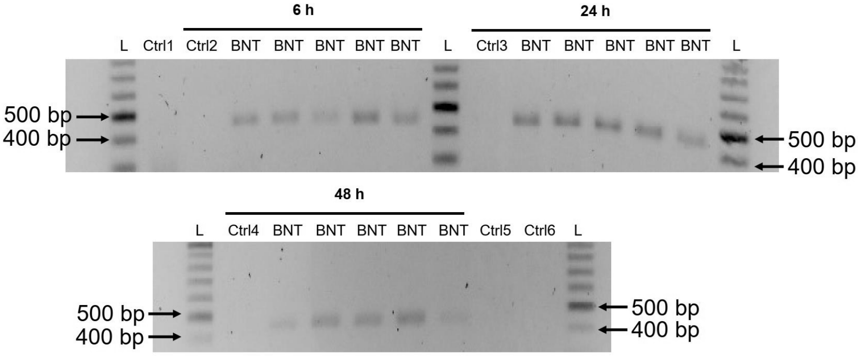



**Figure 6.2** Detection of copies of the spike protein gene encoded by the Pfizer vaccine within the cellular DNA of a human liver cell line (taken from Figure 5 in [257]). The cells were exposed to the vaccine for the lengths of time indicated. Cellular DNA was then isolated, and DNA copies of the vaccine mRNA detected by PCR amplification of a fragment 444 base pairs (bp) in length. All samples labelled with 'BNT' had been treated with the vaccine. Each of them shows a PCR product of the expected length, as is evident from comparison to a DNA fragment length standard ('L'). Samples labelled with 'Ctrl *n*' were controls: Ctrl 1–4 contained DNA from cells not incubated with vaccine, Ctrl 5 contained RNA (not DNA) from vaccine-treated cells, and Ctrl 6 the same but additionally treated with RNAse, which step was also performed in the purification of DNA samples. As expected, none of the control samples yield the PCR product.

**6.2.7 Detection of intracellular DNA encoding spike protein does not distinguish between retrotransposition and direct transfection.** We must, however, note one important caveat with the interpretation of the study by Aldén et al.: it does not consider the possibility that the DNA copies which were detected in the cells *were contained in the vaccine as such*, and that their appearance within the cells reflected merely the cellular uptake ("transfection") of such preexisting DNA copies. If the vaccine batch used in Aldén's study indeed contained such contaminating DNA, then its uptake into the cells would very likely have been facilitated by the lipid nanoparticles in the same way as that of the mRNA. Recently reported findings indicate that this possibility must be taken seriously (see Section 6.3).

**6.2.8 Conclusion.** While the findings reported so far with the COVID-19 mRNA vaccines don't definitely prove the reverse transcription of the vaccine mRNA and its genomic insertion in vivo, there is enough circumstantial evidence to show that this risk cannot be dismissed out

of hand. The latter also applies to any and all future mRNA vaccines directed against other pathogenic microbes.

## 6.3 Contaminating plasmid DNA in Pfizer's and Moderna's mRNA vaccines

While the mRNA itself and the cationic lipids are necessary ingredients of any mRNA vaccine, such a vaccine should ideally be free of any contaminating DNA. However, DNA is necessary in the large-scale production of the vaccine mRNA. With Pfizer's and Moderna's COVID-19 vaccines, a DNA copy of the spike protein gene serves as the template for the enzymatic synthesis of the mRNA, which is carried out by an RNA polymerase derived from the *E. coli* bacteriophage T7. This DNA copy is carried on a *plasmid*, that is, a ring-shaped DNA molecule that is able to persist and multiply within bacterial cells. Large amounts of plasmid DNA can easily be obtained from liquid cultures of bacteria that contain the plasmid in question.

Since DNA is chemically quite similar to RNA, lipid mixtures which encase mRNA will do the same with DNA molecules. Thus, in order to prevent the contamination of an mRNA vaccine with the template DNA used for its production, it is necessary to remove the DNA before the mRNA is combined with the lipids. This is possible in principle, but the purification methods used by Pfizer and Moderna seem to have been very unreliable. Of note, the EMA criticized both companies for not having satisfactorily proven the effectiveness of their purification steps [58, 60], but it nevertheless recommended that authorization be granted both manufacturers, without having compelled them to remedy this situation. Furthermore, it appears that once vaccine production had commenced, no process quality control data pertaining to the residual DNA content in the mRNA vaccines were ever demanded from or submitted by the manufacturers to the EMA and other regulators; or at least no such data are in the public domain.

In view of the foregoing, one might not be too surprised to find that the DNA content of the mRNA vaccine exceeded the limit set by the EMA, namely, that DNA should constitute no more than 1 part in 3030 of the total nucleic acids contained in the vaccines. But the sheer amount of the excess DNA contained in some of the vaccine batches is nevertheless astounding. Kevin McKernan, a well-known molecular biologist and pioneer of DNA sequencing methods, found some batches to be contaminated with as much as 20-35% of residual plasmid

DNA [225], which means that EMA's arbitrary limit was exceeded by approximately 1000 times.

The biological and medical risks posed by this contamination have been discussed in detail elsewhere [259]. They are essentially the same as those implied by the reverse transcription and insertion of the mRNA itself; therefore, both will be discussed in parallel below. We stress again that this contamination should be avoidable in principle, and that it might indeed be avoided with future mRNA vaccines against other viruses or pathogenic microbes. However, its presence in both Pfizer's and Moderna's products suggests that currently the problem has not been solved effectively with respect to large-scale production.

## 6.4 Known and plausible risks posed by DNA copies of non-self genes

Sections 6.2 and 6.3 above imply that cells which have taken up mRNA vaccine particles may have to contend not only with the mRNA itself, but also with DNA copies of the vaccine-encoded non-self gene, which in case of the COVID-19 mRNA vaccines means the spike protein gene. As we have seen, such DNA copies may arise either through reverse transcription within the cell, or they may already be contained as process-related contaminations within the vaccine itself.

**6.4.1 Chromosomal integration of the non-self gene.** The mechanism by which mRNA copies may be copied into DNA and concomitantly inserted into our cells' chromosomal DNA was discussed in Section 6.2.3. Plasmid DNA may insert into chromosomal DNA, too [260], and this effect has been widely exploited in the generation of transgenic cells and organisms. More commonly, however, plasmid DNA that was taken up by a body cell will persist within that cell independently, and it is often lost when the cell divides. Nevertheless, considering that a very large number of people have received mRNA vaccines, which apparently were contaminated with significant amounts of plasmid DNA, insertion events must be presumed to have occurred in at least some cases (see also Section 6.4.2.3 below).

**6.4.2 Biological consequences of DNA insertion.** With LINE-1 [243] and most likely with other retrotransposons as well, DNA insertions apparently occur in random locations, but they will occur preferentially within or near transcriptionally active genes, since the DNA of inactive genes will be tightly packed into complexes with histone proteins and

therefore poorly accessible. Insertion of plasmid DNA, too, appears to occur at random sites [261, 262]. Such rancom insertion events may produce different functional effects on the host cell's genome.

**6.4.2.1 Gene inactivation.** Insertion may occur within a gene and disrupt it. This can lead to the loss of important cellular gene products (i.e., proteins) and thus, potentially, to the development of disease including cancer [244, 245]. Insertion may also be accompanied by the deletion of large gene fragments [263].

**6.4.2.2 Gene regulation.** Transcriptional and epigenetic regulation mechanisms may be affected, thus modulating protein expression levels upward or downward with unpredictable and undesirable results. Indirect regulatory effects may affect even distant genes located on other chromosomes, mediated by altered DNA methylation [264].

**6.4.2.3 Activation of oncogenes.** This is a special case of the preceding point, but it is important enough to be highlighted separately. The occurrence of malignancies through DNA integration and activation of cancer-promoting genes (oncogenes) has been demonstrated in clinical trials with a retroviral vector for the genetic treatment of children with SCID-X1 (severe combined immune deficiency) [265]. These malignancies will typically become manifest only several years after the completion of treatment [266]. Therefore, for a valid benefit-risk analysis, long-term surveillance of possible genotoxic effects of chromosomal integration are absolutely indispensable in both preclinical and clinical trials.

Retroviral vectors are especially designed for efficient integration into the host cell genome, since only such stable integration will permanently repair the gene defect in question. With plasmid vectors, the rate of insertion will typically be several orders of magnitude lower. Nevertheless, chromosomal insertion of plasmid DNA has been demonstrated in vivo [262]. In the latter study, intramuscular injection of the plasmid DNA was followed by electroporation. While electroporation did increase the cellular uptake of the injected DNA relative to the injection of "naked" DNA alone, it was likely much less effective in this regard than the lipid nanoparticles contained in an mRNA vaccine would be. Accordingly, we must expect some extent of chromosomal integration of contaminating plasmid DNA in vivo, inside the cells of our own body.

**6.4.3 Plasmid DNA may immortalize cell cultures.** When cells are isolated from a healthy human or animal organ and grown in cell culture, they will divide for a limited number of generations and then die. In contrast, cells derived from malignant tumors and leukemias can be propagated indefinitely. An change similar to that which turns healthy body cells into cancerous ones may also occur in cultured cells, which thereby become immortalized and typically also lose some features that are characteristic of their tissue of origin. This *transformation* is most readily induced by infecting them with oncogenic viruses. However, it has in some cases also been reported to occur with plasmids which do not contain any specific oncogenic activity [267, 268]. These cases must have arisen from the disruption or dysregulation of cellular genes involved in controlling proliferation. Molecular events similar to those which underlie such disruption must also be expected to occur with vaccine-derived DNA inside our own body cells. Thus, in conclusion, within a large enough vaccinated population, the risk of malignancy due to the insertion of vaccine-derived DNA into the chromosomal DNA must be taken seriously.

**6.4.3.1 Expression of the inserted gene.** Integration of the spike protein gene into the host cell could lead to its permanent expression. The consequences will be discussed separately below.

**6.4.3.2 Germline integration.** We noticed above that Pfizer's own animal data indicate a high level of vaccine accumulation in the ovaries (see Section 5.2.1). Furthermore, LINE-1 and other retrotransposons are active and cause genomic insertion events in human oocytes [247]. In combination, these findings indicate that the mRNA gene sequences may be integrated into the DNA of oocytes, and hence into the human germline. The same is possible with contaminating DNA sequences contained in the vaccines as such. Insertion into male germline cells cannot be ruled out either, even though in the animal study discussed in Section 5.2.1 the accumulation of vaccine in the testes was significantly lower than in the ovaries.

Should this indeed come to pass—should the germline cells of vaccinated individuals be rendered transgenic—then the risk of engendering transgenic children will not be limited to these individuals only, but it will necessarily be shared by their current or future spouses. In effect, an entire generation of future parents will be exposed to this risk.

**6.4.4 Persistent expression of the foreign antigen.** While the vaccine mRNA alone will be sufficient for driving the expression of the encoded antigen, this expression should be short-lived. In-vitro data suggest that the modification with methyl-pseudouridine does not significantly extend the duration of that expression, even though it substantially increases the amounts of the encoded antigen produced while the mRNA persists [56, 57].

DNA, including extraneous recombinant DNA, has a much longer lifetime than mRNA. Plasmids engineered to express coagulation factor IX (a plasma protein) have been found to persist in the liver cells of experimental animals at stable levels for up to 1.5 years [269, 270], which was the entire duration of those experiments. Of note, this expression does *not* require the integration of those plasmids into the cellular DNA; the plasmids tend to persist within the cell as long as the latter does not divide, although they may get lost rapidly once cell division is induced [271].

Is there any reason to assume that plasmid-driven expression has occurred with the currently used COVID-19 mRNA vaccines? We noted earlier that the in vitro transcription used in the production of these vaccines is carried out with T7 RNA polymerase. Transcription is initiated when this polymerase binds a cognate T7 *promoter*, a DNA sequence motif which is recognized by and activates the polymerase. In our body cells, mRNA synthesis is carried out by a different enzyme (RNA polymerase II). It has, however, been experimentally confirmed that the T7 promoter also binds this cellular enzyme, and that this causes transcription within mammalian cells [272].

Another line of evidence concerns the duration of spike protein expression observed after vaccination. It is clear from multiple studies on vaccinated individuals that both the spike protein itself and nucleic acids encoding it can be detected, in the bloodstream and in various organs, for weeks and even months after the injection (see Section 5.2.3.1). This discrepancy between in vitro and in vivo studies has so far been difficult to understand. Long-term persistence of plasmid DNA, and expression of spike protein from it, offers a plausible explanation for these findings.

Long-term expression is also possible with plasmid-derived DNA that has been chromosomally inserted. Reverse transcription and chromosomal insertion of mRNA might give rise to persistent expression, too. Note, however, that the mRNA does *not* contain a copy of the T7

promoter, or any other promoter that could drive the transcription of a DNA copy. Thus, in this case, the promoter would have to be supplied by the chromosomal DNA in the vicinity of the inserted gene. While this is not impossible, it seems less likely to occur in practice than expression from a contaminating DNA copy contained in the vaccine.

In Chapter 4, we have seen that the expression of spike protein correlates with destructive autoimmune-like inflammation against the cells and tissues in question. The prolonged expression of spike protein driven by DNA copies of the gene would therefore extend the duration and increase the cumulative destructive effects of such inflammation.

# 7. Epidemiology of COVID-19 mRNA Vaccine Adverse Events

Margot DesBois, B.A. and Brian S. Hooker, Ph.D.[1]

## 7.1 Introduction

The FDA first authorized the use of SARS-CoV-2 mRNA vaccines under Emergency Use Authorization in December 2020 [273]. Between then and December 2022, over 650 million doses of mRNA COVID-19 vaccines were administered in the U.S. and nearly 13 billion worldwide [274]. Since the rollout of this vaccination program, individuals and health care practitioners have reported millions of adverse events following vaccination with the novel Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines. Despite repeated government health agency claims that these vaccines are safe for virtually all children and adults, numerous epidemiological studies reveal significantly increased incidences of serious health problems following these injections in the U.S. and around the world. This peer-reviewed research includes analyses of clinical trial data, passive surveillance data, and prospective and retrospective cohort data, many of which directly compare vaccinated and unvaccinated groups. Study populations include randomized trial participants, hospital patients, government healthcare enrollees, and public volunteers, from city, health care system, national, and international databases.

## 7.2 General Adverse Events, Serious Adverse Events, Death, Hospitalization, Life-Threatening Events

**7.2.1 Clinical Trial Data Analyses.** Multiple research groups have analyzed data from the randomized, placebo-controlled trials for both

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the Pfizer BNT162b2 and Moderna mRNA-1273 SARS-CoV-2 mRNA vaccines and found significantly higher incidences of adverse events in the vaccinated groups than the unvaccinated groups.

Cheng et al. reviewed multiple literature sources to assess phase III clinical trial data on the different COVID-19 vaccines [275]. In their analysis of eight studies, seven COVID-19 vaccines, and over 150,000 subjects, they found that the mRNA vaccines showed the highest risk of adverse events compared to unvaccinated controls, with 1.83 times (95% CI 1.80-1.86) and 2.16 times (95% CI 2.11-2.20) increased risk of an adverse event after the first and second dose, respectively.

Investigators Kouhpayeh and Ansari also reviewed published clinical trial data, including five mRNA vaccine studies comprising nearly 60,000 subjects each in the vaccine and control groups [276]. They found that receipt of mRNA vaccines was associated with 1.53 times (95% CI 1.08-2.16) greater risk of systemic adverse events compared to unvaccinated groups. The most common types of systemic reactions reported were fever, fatigue and headache.

Fraiman et al. assessed serious adverse events (SAE) and serious adverse events of special interest (AESI) in phase III clinical trial data for the Pfizer BNT162b2 and Moderna mRNA-1273 vaccines [277]. They used SAE that were listed within each trial and derived AESI from a priority list of adverse events created by the Brighton Collaboration and endorsed by the World Health Organization. A SAE was defined as

> *death, life-threatening at the time of the event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, a congenital anomaly/birth defect, or a medically important event, based on medical judgment.*

Combined, the two mRNA vaccines were associated with an excess risk of AESI of 12.5 per 10,000 vaccinated (95% CI 2.1-22.9). Trial participants vaccinated with either vaccine had a 43% higher risk of AESI than controls (risk ratio 1.43; 95% CI 1.07 to 1.92).

Pfizer trial participants who received the vaccine exhibited a 36% higher risk of SAE than controls (risk ratio 1.36, 95% CI 1.02-1.83; risk difference 18.0 per 10,000 vaccinated, 95% CI 1.2-34.9), in contrast to the FDA's conclusion that SAEs were "balanced between treatment groups" [277, 278]. Possible reasons for this discrepancy include the FDA's use of a different analysis population and shorter follow-up windows. Also, while the FDA analyzed the total number of participants

experiencing any SAE, Fraiman et al. based their analyses on the total number of SAEs. In both Pfizer and Moderna trials, Fraiman et al. found that the largest excess risk occurred among the Brighton category of coagulation disorders.

Fraiman et al. also completed a risk-benefit assessment of both vaccines and found that the Pfizer BNT162b2 vaccine showed an excess risk of serious AESI of 10.1 per 10,000 vaccinees, while preventing COVID-19 hospitalizations in 2.3 per 10,000 vaccinees, compared to the placebo group. The Moderna mRNA-1273 vaccine showed an excess risk of serious AESI of 15.1 per 10,000 vaccinees while preventing COVID-19 hospitalizations in 6.4 per 10,000 vaccinees, compared to the placebo group [277].

**7.2.2 Post-Marketing Surveillance Data Analyses.** Investigators also discovered higher incidences of certain adverse events through analyses of pharmacovigilance data collected in the months following the rollout of vaccines to the public.

An FDA-sponsored prospective study by Wong et al. assessed U.S. Medicaid claims data for over 30 million patients aged 65 years and older from December 2020 through January 2022 [279]. Researchers compared the observed number of 14 different outcomes in patients who received at least one dose of a COVID-19 vaccine to an expected number based on the background rate in a similar COVID-19 unvaccinated population prior to the pandemic. Weekly sequential testing revealed four outcomes that met the threshold for a statistical signal following Pfizer BNT162b2 vaccination: pulmonary embolism (PE; rate ratio 1.54; 1-28 days post-vaccination), acute myocardial infarction (AMI; rate ratio 1.42; 1-28 days), disseminated intravascular coagulation (DIC; rate ratio 1.91; 1-28 days), and immune thrombocytopenia (ITP; rate ratio 1.44; 1-42 days). After adjustment for monthly variation in the background rates, only the rate ratio for PE still met the statistical threshold for a signal [279].

Between December 2020 and December 2022, the Vaccine Adverse Event Reporting System (VAERS) received and processed over 2.5 million reports related to COVID-19 vaccines, a reporting rate of about 42 per 10,000 doses [280, 281]. These included 40,883 reports of death associated with an mRNA COVID-19 vaccine, equivalent to about 6 deaths per 100,000 doses administered. This is more than 45 times

**Table 7.1** Relative risks of death, life-threatening reactions (LTR), and hospital admission associated with each of the four major gene-based COVID-19 vaccines, compared to all influenza vaccines combined, for the time period of December 2020 to October 2021. Data from Table 1 in Montano [282]. The AstraZeneca vaccine has not been used in the U.S. and is therefore missing from the VAERS data.

| Database | | EudraVigilance | | | VAERS | | |
|---|---|---|---|---|---|---|---|
| Event severity | | Death | LTR | Hospital | Death | LTR | Hospital |
| COVID vaccine | AstraZeneca | 68 | 135 | 89 | — | — | — |
| | Janssen | 33 | 49 | 35 | 364 | 289 | 242 |
| | Moderna | 97 | 108 | 96 | 403 | 201 | 195 |
| | Pfizer | 30 | 33 | 31 | 299 | 179 | 177 |
| All COVID vaccines | | 43 | 56 | 46 | 345 | 197 | 190 |
| Influenza vaccines (reference) | | 1 | 1 | 1 | 1 | 1 | 1 |

the rate of deaths reported for all the influenza vaccines since 1990 combined.

In his surveillance data analysis of EudraVigilance (The European Database of Suspected Adverse Drug Reactions) and VAERS post roll-out in 2020 to October 2021, Montano compared rates of adverse event reports for COVID-19 vaccines to those for influenza vaccines [282]. He estimated the total number of each type of vaccine administered using vaccine coverage data in Europe and the U.S. from the European Centre for Disease Prevention and Control (ECDC), the European Statistical Office (Eurostat) and the Centers for Disease Control and Prevention (CDC). Death, hospitalization, and life-threatening reaction reports per unit of COVID-19 vaccine (including AstraZeneca, Janssen, Moderna and Pfizer) given far eclipsed those for the influenza vaccines. In EudraVigilance and VAERS, respectively, the number of death reports were 42.53 times (95% CI 33.49-54.01) and 345.42 times (95% CI 224.61-531.20) greater, the number of hospitalization reports were 45.71 times (95% CI 41.26-50.65) and 189.65 times (95% CI 163.85-219.53) greater, and the number of life-threatening reaction reports were 56.13 times (95% CI 44.51-70.78) and 196.72 times (95% CI 147.04-263.19) greater. Table 7.1 summarizes these findings.

While all COVID-19 vaccines greatly exceeded the risk of adverse events associated with the influenza vaccines, there nevertheless were some differences between them. In EudraVigilance, the Moderna vac-

cine alone was associated with 2.99 times (95% CI 2.69-3.32) more frequent reporting of death, 2.77 times (95% CI 2.65-2.89) more frequent reporting of hospitalization, and 2.20 times (95% CI 2.02-2.39) more frequent reporting of life-threatening reactions than the Janssen vaccine. However, this pronounced difference was not apparent in VAERS. The largest relative risks for COVID-19 vaccines compared to influenza vaccines were found for allergic reactions, arrhythmia, general cardiovascular events, coagulation, hemorrhages, gastrointestinal reactions, ocular reactions, sexual organ reactions, and thrombosis.

**7.2.3 Vaccinated vs. Unvaccinated Cohort Analysis.** Other investigators found increased adverse events in a clinical post-marketing setting. Barda et al.'s retrospective cohort study included about 800,000 matched vaccinated and unvaccinated patients from a large healthcare organization in Israel. Their results showed that compared to unvaccinated patients, patients receiving the Pfizer BNT162b2 vaccine between December 2020 and May 2021 had elevated risk of myocarditis (risk ratio 3.24; 95% CI 1.55-12.44; risk difference 2.7 events per 100,000 persons; 95% CI 1.0- 4.6), lymphadenopathy (risk ratio 2.43; 95% CI 2.05-2.78; risk difference 78.4 events per 100,000 persons; 95% CI 64.1-89.3), appendicitis (risk ratio 1.40 95% CI 1.02-2.01; risk difference 5.0 events per 100,000 persons; 95% CI 0.3-9.9), and herpes zoster infection (risk ratio 1.43; 95% CI 1.20-1.73; risk difference 15.8 events per 100,000 persons; 95% CI 8.2-24.2) [283].

**7.2.4 Summary.** Researchers investigating the scope of adverse events following COVID-19 mRNA vaccination have found increased incidences of adverse events in general; serious adverse events, including coagulation disorders; pulmonary embolism, acute myocardial infarction, disseminated intravascular coagulation, and immune thrombocytopenia in those 65 years and older; allergic reactions; arrhythmia; general cardiovascular events; coagulation; hemorrhages; gastrointestinal reactions; ocular reactions; sexual organ reactions; thrombosis; myocarditis; lymphadenopathy, appendicitis; herpes zoster infection; hospitalization; life-threatening reactions; and death.

## 7.3 Cardiac Events

Inflammatory heart problems have been strongly associated with mRNA COVID-19 vaccination in numerous analyses of passive surveillance, active surveillance, and health care system cohort data.

**7.3.1 Surveillance Data Analyses.** Early documentation linking myocarditis to the mRNA COVID-19 vaccines occurred in a U.S. Department of Defense study, published in June 2021, detailing 23 cases in U.S. military service personnel between January and April 2021 [284]. By the week of February 19th 2021, VAERS had received sufficient serious adverse event reports to implicate myocarditis in young males as causally connected to the COVID-19 vaccines with greater than 95% confidence [285]. Despite this available evidence of harm, on May 10, the FDA expanded the EUA for the Pfizer-BioNTech vaccine to include the 14 million Americans ages 12 through 15 years [286]. The CDC approved and recommended the vaccine to this age group two days later [287]. On May 27th, the CDC acknowledged adverse cardiac responses to vaccination, creating the webpage "Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination" on its website and stating [288]:

> *Since April 2021, there have been increased reports to the Vaccine Adverse Event Reporting System (VAERS) of cases of inflammation of the heart.*

Between December 2020 and December 2022, over 4,000 (~ 0.16%) of the VAERS reports filed for COVID-19 vaccines were reports of myocarditis, 100 times as many events per vaccine dose as for influenza [280, 281].

Oster et al.'s descriptive analysis of VAERS reports of myocarditis after mRNA vaccination between December 2020 and August 2021 found 1,626 reports that met the case definition of myocarditis [289]. The risk was highest after the second dose in adolescent males aged 16 to 17 years (105.9 [95% CI 91.65-122.27] per million doses of the Pfizer BNT162b2 vaccine), in adolescent males aged 12 to 15 years (70.7 [95% CI 61.88-81.11] per million doses of the Pfizer BNT162b2 vaccine), and in young men aged 18 to 24 years (52.4 [95% CI 45.56-60.33] and 56.3 [95% CI 47.08-67.34] per million doses of the Pfizer BNT162b2 and the Moderna mRNA-1273 vaccines, respectively). Figure 7.1 depicts some key findings from this study.

A VAERS analysis of myocarditis and pericarditis following vaccination with any COVID-19 vaccine by Li et al., using the same observation period (December 2020 to August 2021), found a lower incidence rate of 5.98 cases per million doses administered (95% CI 5.73-6.24) [290]. The incidence rate was the highest in adolescents aged 12 to 17 years, at 20.94 (95% CI 19.01–23.01) per million doses. Reports were more

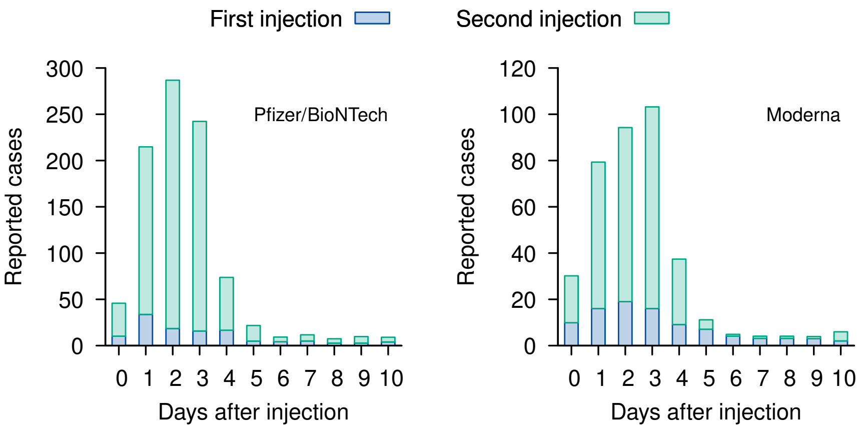



**Figure 7.1** Cases of myocarditis after COVID-19 mRNA vaccination reported to VAERS between December 2020 and August 2021, by day of onset after vaccination and manufacturer. Replot of Figure 2 in [289].

common after the administration of the second dose of mRNA vaccines than the first. Overall, compared to all other vaccines in VAERS, the two mRNA COVID-19 vaccines were associated with increased odds for myocarditis/pericarditis, with reporting odds ratios of 2.91 (95% CI 2.21–3.83) for Moderna mRNA-1273 and 5.37 (95% CI 4.10–7.04) for Pfizer BNT162b2.

Straus et al.'s post-marketing surveillance analysis of the Moderna global safety database from December 2020 to February 2022 revealed that rates of myocarditis post-vaccination with the Moderna vaccine were highest for males aged less than 40 years, particularly those 18–24 years (53.76 per 100,000 person-years), which was 3.10 times higher (95% CI 2.68–3.58) than an expected rate from a population-based data estimate from the U.S. Premier Healthcare Database [291].

Witberg et al.'s retrospective cohort analysis of over 2.5 million vaccinated patients in a large Israeli health care system found that of those who had received at least one dose of the Pfizer BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 100,000 persons (95% CI 1.56-2.70) [292]. The highest incidence was among male patients between the ages of 16 and 29 years (10.69 cases per 100,000 persons; 95% CI 6.93-14.46), comparable to Oster at al.'s findings.

Krug et al.'s risk-benefit analysis using VAERS data found that in boys with prior COVID-19 infection and no comorbidities, even one dose of Pfizer BNT162b2 vaccine carried more risk of myocarditis/pericarditis than benefit against COVID-19 hospitalization during the delta wave in 2021, according to international estimates [293].

Chua et al.'s retrospective population cohort study covering June through September 2021 [294] found an incidence rate of acute myocarditis/pericarditis following vaccination with a second dose of Pfizer Comirnaty in Chinese male adolescents aged 12-17 of 37.32 per 100,000 individuals vaccinated (95% CI 26.98–51.25).

In Kim et al.'s surveillance analysis of the WHO VigiBase database [295], the investigators compared cardiac adverse events from the mRNA COVID-19 vaccines to those from the influenza vaccine, reported from January 2020 to January 2021. Individuals receiving COVID-19 mRNA vaccines showed significantly higher reporting odds for the cardiac adverse events of hypertensive crisis (12.72 times; 95% CI 2.47–65.54) and supraventricular tachycardia (7.94 times; 95% CI 2.62–24.00) compared with the influenza vaccine, per dose administered.

An analysis of a dataset from Israel's National Emergency Medical Services (EMS) by Sun et al. found an over 25% increase in cardiac arrest and acute coronary syndrome EMS calls in the 16–39-year-old population during January–May 2021, compared with the years 2019–2020 [296]. The weekly emergency call counts were significantly correlated with the rates of first and second vaccine doses administered to this age group but were not associated with COVID-19 infection rates.

**7.3.2 Vaccinated vs. Unvaccinated Cohort Analyses.** In a meta-analysis of four national cohort studies assessing participants 12 years and older within 28 days of vaccination over the period of December 2020 through October 2021, Karlstad et al. observed the highest risk of myocarditis in males between 16 and 24 years of age after receiving the second dose of mRNA vaccine: 5.31 times (95% CI 3.68-7.68) higher for Pfizer and 13.83 times (95% CI 8.08-23.68) higher for Moderna, compared to unvaccinated individuals [297].

In Mevorach et al.'s retrospective cohort study of Israeli Ministry of Health data, the incidence of myocarditis within 30 days after the second dose of the Pfizer BNT162b2 mRNA vaccine was 2.35 times (95% CI 1.10-5.02) higher than in unvaccinated people [298]. The rate ratio was highest in male recipients between the ages of 16 and 19

years, at 8.96 times (95% CI 4.50-17.83) higher, with an incidence in this group of 1 in 6,637. This is 1.64 times higher than the incidence rate of myocarditis that these researchers calculated in the general unvaccinated population (1 in 10,857). Within 30 days of receiving the second vaccine dose, incidence of myocarditis was 5.34 times (95% CI 4.48-6.40) higher than the expected incidence based on historical data from the Israel National Hospital Discharge Database, 2017-2019. Again, the risk was highest in male recipients between the ages of 16 and 19 years, at 13.60 times (95% CI 9.30-19.20) higher, representing 32 observed cases, compared to 2.35 expected cases.

Lai et al.'s retrospective cohort study of adolescents aged 12–18 in a Hong Kong healthcare database, which included over 200,000 patients, assessed incidence of adverse events within 28 days of receiving the Pfizer BNT162b2 vaccine [299]. Participants who received the first dose of the vaccine had 9.15 times (95% CI 1.14–73.16) greater risk of myocarditis compared to unvaccinated adolescents, and those who received the second dose had 29.61 times (95% CI 4.04–217.07) greater risk. In addition, after the second dose, vaccinated adolescents had 2.06 times (95% CI 1.01–4.24) greater risk of sleep disturbances/disorders compared to unvaccinated adolescents.

Lai et al.'s case-control study of hospitalized patients in Hong Kong from February to August 2021 assessed 160 patients with carditis and elevated troponin levels and 1,533 control patients [300]. Multivariable analyses controlling for cardiovascular disease risk factors showed that recipients of the Pfizer BNT162b2 vaccine had 3.57 times greater odds (95% CI 1.93-6.60) of carditis than unvaccinated patients. For male vaccine recipients, the odds were 4.68 times greater (95% CI 2.25-9.71). The risk was higher after the second dose of BNT162b2 than the first.

**7.3.3 Other Cohort Analyses.** Goddard et al. performed a retrospective analysis of CDC's Vaccine Safety Datalink database of eight integrated healthcare delivery systems [301]. The study was coauthored by CDC's Immunization Safety Office Director Dr. Tom Shimabukuro and CDC colleagues Dr. Eric Weintraub and Dr. Matthew Oster. They found that participants aged 18-39 showed significantly greater risk of myocarditis or pericarditis within 7 days of receiving the first or second dose of the Pfizer or Moderna COVID-19 vaccines in a period from December 2020 to January 2022, compared with that of those vaccinated 22 to 42 days earlier. For the Pfizer vaccine the incidence

was 3.02 times (95% CI 1.03–8.33) higher after the first dose and 14.30 times (95% CI 6.45–34.85) higher after the second dose, and for the Moderna vaccine the incidence was 3.46 times (95% CI 1.12–11.07) higher after the first dose and 18.75 times (95% CI 6.73–64.94) higher after the second dose.

Simone et al.'s retrospective cohort study included patients within the Kaiser Permanente Southern California database who received one to three doses of mRNA COVID-19 vaccines between December 2020 and February 2022, a total of over 3 million individuals [302]. The risk of myocarditis within 7 days or the second vaccine dose was 10.23 times (95% CI 6.09–16.4) higher than in the 365-day baseline period, two years before the vaccination date. The risk of myocarditis within 7 days of the third vaccine (booster) dose was 6.08 times (95% CI 2.34–13.3) higher. There was no statistically significant risk associated with the first mRNA vaccine received in this study.

In Massari et al.'s self-controlled case series study using Italian national hospital data between December 2020 and September 2021, males aged 12-39 receiving the Moderna vaccine had a 12.28 times (95% CI 4.09-36.83) greater risk of myocarditis or pericarditis diagnosis within 7 days of vaccination with dose one and an 11.91 times (95% CI 3.88-36.53) greater risk after dose two, compared to the baseline period excluding the interval of 0 to 21 days after the first or second vaccine doses [303].

Patone et al.'s self-controlled case series study considered diagnosis of myocarditis in individuals ages thirteen or older in England between December 2020 and December 2021 [304]. Men showed elevated risk within 28 days following doses one (2.35 times; 95 % CI 1.09–5.08), two (14.98 times; 95% CI 8.61–26.07), and three (3.57 times; 95% CI 1.48–8.64) of the Moderna vaccine, compared to the baseline period outside the window spanning 29 days before and 29 days after vaccination. The highest incidence, occurring in men under the age of forty years, was 16.83 times (95% CI 9.11–31.11) increased risk, occurring within 28 days of vaccination with a second dose. There was also significantly increased incidence for all participants receiving any dose of Pfizer, and doses two and three of Moderna; women receiving doses one or three of Pfizer and dose two of Moderna; and men receiving any dose of Pfizer.

**7.3.4 Summary.** Myocarditis is a serious illness, indicating damage to the myocardium (heart muscle wall). Individuals at the highest risk comprise young men, although females may contract myocarditis as well. Almost 20% of all sudden deaths in young people are due to myocarditis. The survival rate is 80% after one year and 50% after five years [305].

The preceding analyses confirm a significant presence of myocarditis in mRNA vaccine recipients, highest in adolescent and young adult males. Compared to all other vaccines in VAERS, the mRNA COVID-19 vaccines were associated with increased odds of myocarditis/pericarditis. The incidence of myocarditis ranged from under 10 cases per million to over 100 cases per million doses of vaccine. Compared to unvaccinated or baseline rates, myocarditis incidence was about two to nearly 30 times greater for the vaccinated, depending on age, sex, and vaccine type. Rates were usually higher after the second dose than the first. In contrast, COVID-19 infection (defined by positive PCR test) was not associated with either myocarditis (adjusted hazards ratio (aHR) 1.08; 95% CI 0.45-2.56) or pericarditis (aHR 0.53; 95% CI 0.25-1.13) in a large retrospective cohort study of nearly 200,000 adults in Israel between March 2020 and January 2021 [306]. In addition to myocarditis, individuals receiving the mRNA vaccines had increased odds of the cardiac adverse events hypertensive crisis and supraventricular tachycardia, compared with influenza vaccine recipients.

## 7.4 Thrombotic Events

Blood clotting disorders in the vasculature of the body and the brain following mRNA COVID-19 vaccination have been quantified and assessed in observational and self-controlled studies. While cerebrovascular events made up less than 0.1% of the COVID-19 vaccine VAERS reports, there were over 60 times as many cerebrovascular events per dose reported for COVID-19 vaccines as for the influenza vaccine [280, 281].

An observational cohort study by Tu et al. of all public acute hospitals in Singapore between January 2020 and August 2021 found nine patients hospitalized with cerebral venous thrombosis (CVT) within 6 weeks after mRNA SARS-CoV-2 vaccination (Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273) [307]. This amounted to a crude incidence rate of 2.59 per 100,000 person-years (95% CI 1.19-4.92).

Hippisley-Cox et al.'s self-controlled case series study analyzed hospital admissions and deaths among a pool of about 30 million

people vaccinated with a COVID-19 vaccine between December 2020 and April 2021 in the UK register [308]. The researchers compared participants 0-28 days post-vaccination to a baseline period excluding the window 28 days prior to vaccination and 28 days post-vaccination. Vaccination with one dose of the Pfizer vaccine was associated with 1.06 times (95% CI 1.01 to 1.10 at 15-21 days) increased risk of arterial thromboembolism, 3.58 times (95% CI 1.39 to 9.27 at 15-21 days) increased risk of cerebral venous sinus thrombosis, and 1.12 times (95% CI 1.04 to 1.20 at 15-21 days) increased risk of ischemic stroke.

In Berild et al.'s retrospective self-controlled cohort study, investigators used hospital registries from Norway, Finland, and Denmark between January 2020 and May 2021 to compare the incidence of thrombocytopenic and thromboembolic events within a 28-day period following COVID-19 vaccination to a baseline period prior to vaccination [309]. They found a 1.13 times (95% CI 1.02-1.25) increased rate of coronary artery disease following Moderna vaccination, and 1.12 times (95% CI 1.07-1.19) and 1.26 times (95% CI 1.07-1.47) increased rates of coagulation disorders following Pfizer and Moderna vaccination, respectively [309]. They also observed increased rates of cerebrovascular disease following Pfizer (1.09 times; 95% CI 1.05-1.13) and Moderna (1.21 times; 95% CI 1.09-1.35) vaccination.

**7.4.1 Summary.** In addition to Wong et al.'s surveillance study findings associating Pfizer BNT162b2 vaccination with thrombotic conditions of pulmonary embolism, disseminated intravascular coagulation, and immune thrombocytopenia in patients 65 years and older, mRNA COVID-19 vaccines are linked to cerebral venous thrombosis, arterial thromboembolism, ischemic stroke, coronary artery disease, coagulation disorders, and cerebrovascular disease.

## 7.5 Neurological Events

Dutta et al.'s disproportionality analysis of the WHO's VigiBase surveillance data found that the neurological adverse events associated with the administration of the COVID-19 vaccines included ageusia, anosmia, burning sensation, dizziness, facial paralysis, headache, hypoaesthesia, lethargy, migraine, neuralgia, paresis, parosmia, poor sleep quality, seizure, transient ischemic attack, and tremor [310].

Hosseini et al.'s systematic review of adverse neurological effects found evidence that the mRNA vaccines are linked to headache; de-

myelinating disorders including transverse myelitis, multiple sclerosis, and neuromyelitis optica; small fiber neuropathy; Parsonage-Turner syndrome; Guillain Barré syndrome; Bell's palsy; abducens nerve palsy; acute disseminated encephalomyelitis; encephalopathy; olfactory dysfunction and phantosmia; tinnitus and cochleopathy; akathisia; seizures; epilepsy; delirium; and cerebrovascular disorders including cerebral venous sinus thrombosis, intracerebral hemorrhage, ischemic stroke, and transient ischemic attack [311].

**7.5.1 Hemorrhagic Stroke.** Patone et al.'s self-controlled case series study used UK data from the National Immunisation Management Service (NIMS) database to investigate hospital admissions from neurological complications in the 28 days after a first dose of Pfizer BNT162b2, including over 12 million recipients between December 2020 and May 2021 [312]. Compared to baseline rates outside the 28-day window following vaccination (pre-vaccination and after day 28), patients who had received the vaccine had 1.38 times (95% CI 1.12–1.71 at 15–21 days) increased risk of hemorrhagic stroke.

**7.5.2 Bell's Palsy.** In Sato et al.'s VAERS disproportionality analysis, spanning January 2010 through April 2021, the Pfizer and Moderna vaccines showed increased incidences of Bell's palsy of 1.84 times (95% CI 1.65–2.06) and 1.54 times (95% CI 1.39–1.70), respectively, compared to all other vaccines [313].

Shibli et al.'s retrospective cohort study retrieved data on Pfizer BNT162b2 mRNA COVID-19 vaccination from the database of the largest healthcare provider in Israel, for the time period from December 2020 through April 2021, which comprised over 2.5 million vaccine recipients [314]. Patients were counted as cases of Bell's palsy if they had been diagnosed and assigned the appropriate ICD coding within 21 days of the first vaccine dose or within 30 days of the second vaccine dose, and furthermore had filled a prescription of prednisone [315] within two weeks of the diagnosis. The numbers were compared to the expected cases, based on 2019 rates. The first vaccine dose was associated with 1.36 times increased risk of Bell's palsy (95% CI 1.14-1.61). Risk was higher in older females, with female vaccinees aged 45-64 at 1.71 times (95% CI 1.10-2.54) greater risk, with a rate of 2.58 cases per 100,000 vaccinees, and female vaccine recipients older than 65 years at 2.51 times (95% CI 1.65-3.68) greater risk, with a rate of 4.46 cases per 100,000 vaccinees.

Wan et al.'s self-controlled and case-control analyses used data from population-based electronic health records in Hong Kong to assess diagnosis of Bell's palsy in an inpatient setting within 28 days of Pfizer BNT162b2 vaccination between March and July 2021 [316]. Vaccination was associated with 1.543 times (95% CI, 1.123–2.121) increased odds of Bell's palsy diagnosis compared to matched controls, with up to 1.112 excess events per 100,000 people who received two doses. Compared to controls, they found 2.325 times (95% CI 1.414–3.821) increased odds of Bell's palsy during the first 14 days after the second dose. Their self-controlled case series analysis, which compared Bell's palsy incidence between the 28-day post-vaccination period and a baseline window outside the post-vaccination period (before vaccination and after 28 days post-vaccination) showed 2.44 times (95% CI 1.32–4.50) increased risk of Bell's palsy within 14 days post-vaccination with a second dose.

A review and meta-analysis by Lai et al. included five studies that quantified Bell's palsy, which collectively demonstrated that compared to unvaccinated groups, individuals who received Pfizer BNT162b2 or Moderna mRNA-1273 had 1.36 times increased odds of Bell's palsy (95% CI 1.03–1.79) [317].

**7.5.3 Sensorineural Hearing Loss.** Yanir et al.'s population-based retrospective cohort study of a large health care organization in Israel from December 2020 to May 2021 found that the risk of sudden sensorineural hearing loss was increased 1.35 times (95% CI 1.09-1.65) after the first Pfizer vaccine dose and 1.23 times (95% CI 0.98-1.53) after the second dose, compared to the experience of the population in 2018 and 2019 [318]. Patients were counted as cases of sensorineural hearing loss if they had been diagnosed and assigned the appropriate ICD coding within 21 days of receiving a first or second vaccine dose, and furthermore had filled a prescription of prednisone [43] within 30 days of the diagnosis. Increased risk was greatest after the first dose in females aged 16 to 44 years (1.92 times; 95% CI 0.98-3.43) and females older than 65 years (1.68 times; 95% CI 1.15-2.37) and after the second dose in males aged 16 to 44 years (2.45 times; 95% CI 1.36-4.07). Patients with sudden sensorineural hearing loss can experience permanent hearing loss and tinnitus.

**7.5.4 Summary.** Surveillance data suggest that mRNA COVID-19 vaccines can lead to a host of severe immune-mediated neurological con-

ditions. Short-term analyses have identified hemorrhagic stroke (1.38 times increased risk), Bell's palsy (1.36-2.51 times increased risk), and sensorineural hearing loss (1.35 times increased risk) as associated with vaccination.

## 7.6 Immunological Events

Retrospective cohort analyses have revealed that mRNA vaccines may activate herpes zoster infection, causing shingles.

In an analysis of over one million matched case-control pairs from the global TriNetX database spanning November 2019 through November 2021, Hertel et al. found a 1.802 times (95% CI 1.680-1.932) greater frequency of herpes zoster diagnosis with sixty days of vaccination in those who received at least one mRNA lipid nanoparticle (LNP) or adenovirus vector-based COVID-19 vaccine compared to those who did not receive any COVID-19 vaccine [319]. Pfizer and Moderna mRNA vaccine recipients comprised 98.5% of all COVID-19 vaccine recipients in the study.

Wan et al.'s self-controlled case series and case-control study using Hong Kong Department of Health records between February and July 2021 included over one million Pfizer BNT162b2 vaccine recipients [320]. Patients who received the Pfizer vaccine were 5.23 times (95% CI 1.61–17.03) and 5.82 times (95% CI 1.62–20.91) more likely to be diagnosed with shingles in hospital 0-13 days and 14-27 days after receiving the first dose, respectively, and 5.14 times (95% CI 1.29–20.47) more likely 0-13 days following the second dose, compared to the baseline period of any time outside of the specified time frames surrounding vaccination.

**7.6.1 Summary.** COVID-19 vaccine recipients experienced 1.80-5.82 times higher frequency of herpes zoster diagnosis compared to unvaccinated groups or baseline periods.

## 7.7 Reproductive Events

**7.7.1 Absence of Clinical Trial Pregnancy Data.** The Phase III clinical trials for mRNA COVID-19 vaccines that led to their Emergency Use Authorizations excluded pregnant and breastfeeding women [321, 322]. In February 2021, Pfizer-BioNTech began a phase II/III clinical trial to assess the safety and efficacy of its BNT162b2 vaccine in pregnant women, which ultimately enrolled just 349 participants [323]. To date,

no data from this trial have been published. Pfizer representatives explained that after the U.S. and other governments officially recommended mRNA COVID-19 vaccines to pregnant women in mid- to late-2021, enrollment in this trial declined [324]. The representatives wrote in an email [324]:

> *With the declining enrollment, the study had insufficient sample size to assess the primary immunogenicity objective and continuation of this placebo-controlled study could no longer be justified due to global recommendations. This proposal was shared with and agreed to by FDA and EMA [European Medicines Agency].*

The package insert of the FDA-approved Pfizer Comirnaty vaccine states [325]:

> *Available data on COMIRNATY administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.*

An equivalent disclosure is found in the package insert for the FDA-approved Moderna Spikevax vaccine [326]:

> *Available data on SPIKEVAX administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.*

The CDC nevertheless recommends COVID-19 vaccination [327]

> *for people who are pregnant, breastfeeding, trying to get pregnant now, or might be pregnant in the future.*

However, post-marketing research indicates significant adverse effects on pregnancy, fetal outcomes, and both female and male fertility.

**7.7.2 Passive Surveillance Analyses.** Of all VAERS reports filed for COVID-19 vaccines between December 2020 and December 2022, more than 13,000 (0.50%) were reports of menstrual irregularities [280, 281]. This amounted to 1,000 times as many menstrual irregularities per vaccine dose reported for COVID-19 vaccines as for influenza vaccines. Out of the 224,960 Yellow Card Reports filed in the UK related to the Moderna and Pfizer-BioNTech COVID-19 vaccines combined, 23% (51,695) described menstrual abnormalities [281, 328].

Thorp et al.'s analysis of VAERS data from January 1998 to June 2022 [329] showed that compared to the influenza vaccines, COVID-19 vaccines are associated with significant increases in the pregnancy and menstruation adverse events of menstrual abnormality, miscarriage,

fetal chromosomal abnormalities, fetal malformation, fetal cystic hygroma, fetal cardiac disorders, fetal cardiac arrest, fetal arrhythmias, fetal vascular malperfusion, fetal growth abnormalities, fetal abnormal surveillance, placental thrombosis, fetal death/stillbirth, low amniotic fluid, preeclampsia, premature delivery, preterm premature rupture of membrane, and premature baby death. All proportional reporting ratios for these events exceeded 2.0, the CDC's threshold for a signal of concern, across all three normalization methods: by unit time, by dose given, and by persons vaccinated.

An unpublished analysis of VAERS data as of April 7, 2023 showed that since the introduction of the first COVID-19 vaccines in December 2020, people have reported 3.28 times more spontaneous abortions for COVID-19 vaccines than for all other vaccines over the thirty-two-year history of VAERS (3,576 vs. 1,089 reports), and 13.38 times more fertility problems (19,040 vs. 1,423 reports [330].

A EudraVigilance data analysis by Mascolo et al. reviewed over 3,000 Case Safety Reports related to COVID-19 injections filed by pregnant women during 2021 [281, 331]. Compared to the reports of pregnant women who received non-mRNA COVID-19 vaccines, the reports of those who received mRNA vaccines included nearly twelve times the rate of fetal death (0.81% vs. 0.07%); a higher rate of stillbirths (0.22% vs. 0.17%); almost nine times the rate of hemorrhages during pregnancy (0.62% vs. 0.07%); over three times the rate of fetal disorders (2.5% vs. 0.71%) and of congenital anomalies (0.11% vs. 0.03%); almost four times the rate of premature babies (0.64% vs. 0.17%); and twice the rate of neonatal deaths (0.06% vs. 0.03%).

**7.7.3 Menstrual Survey Analyses.** Lee et al.'s survey of over 39,000 women who received a COVID-19 vaccine from April through June 2021 found that 42% of those with regular menstrual cycles bled more heavily than usual [332]. Among respondents who do not normally menstruate, breakthrough bleeding was reported by 71% of those on long-acting reversible contraceptives, and 66% of postmenopausal women.

Parotto et al. reported a significant increase in self-reported decidual cast shedding (abnormal shedding of the entire uterine lining), amounting to 292 cases, or 4.83% of over 6,000 women who responded to a survey between May and December 2021, compared to 40 pre-pandemic cases reported in the last hundred years [333].

**7.7.4 Vaccinated vs. Unvaccinated Cohort Analyses.** DeSilva et al. described their CDC-funded retrospective matched-cohort study in a letter to the editor of the New England Journal of Medicine [334]. They included pregnant women between the ages of 16 and 49 years at eight Vaccine Safety Datalink sites from December 2020 through July 2021. Of these women, 32,794 (72.5%) had received two doses of an mRNA vaccine. Pregnant women receiving any COVID-19 vaccine, compared to matched, unvaccinated pregnant women, were 2.85 times (95% CI 1.76-4.61) more likely to experience fever, 2.24 times (95% CI 1.71-2.93) more likely to experience malaise or fatigue, 1.89 times (95% CI 1.33-2.68) more likely to sustain local reactions, and 2.16 times (95% CI 1.42-3.28) more likely to experience lymphadenopathy (swollen lymph nodes). The study authors found no difference in serious acute adverse events, and ending the observation period at 42 days after vaccination precluded the evaluation of long-term effects on mother or infant.

Sadarangani et al.'s survey-based observational cohort study included over 90,000 pregnant and non-pregnant women aged 15–49 years in seven Canadian provinces, with over 3,000 pregnant women who received two doses of mRNA vaccine [335]. Pregnant vaccinated women had 4.4 times (95% CI 2.4–8.3) increased odds of a significant health event within 7 days of receiving the second dose of Moderna mRNA-1273, compared with pregnant unvaccinated controls, but not after dose one of Moderna or any dose of Pfizer BNT162b2. The most common significant health events after dose two of mRNA-1273 in pregnant females were feeling unwell or malaise or myalgia, headache or migraine, and respiratory tract infection. In the multivariable analysis adjusting for age group, previous SARS-CoV-2 infection, and trimester, the study found 2.4 times (95% CI 1.3-4.5) increased odds of a significant health event within 7 days after the second dose of any mRNA vaccine, compared with controls.

In a retrospective cohort study by Dick et al. of 5,618 women who delivered between December 2020 and July 2021 at a large tertiary medical center in Israel, those who were vaccinated with either the Pfizer BNT162b2 or Moderna mRNA-1273 vaccine in the second trimester were 1.3 times more likely to have a preterm birth than those who were unvaccinated (8.1% vs. 6.2%; $p < 0.001$). This association persisted after adjusting for potential confounders, with 1.49 times (95% CI 1.11-2.01) greater odds [336].

In Dick et al.'s subsequent study [337], pregnant women who were fully vaccinated and boosted (i.e., triple vaccinated) with either the Pfizer BNT162b2 or the Moderna mRNA-1273 COVID-19 vaccine between July and October 2021 were 2.96 times as likely to experience post-partum hemorrhage as unvaccinated pregnant women (9.5% vs. 3.21%; $p < 0.001$). In addition, practitioners diagnosed triple-vaccinated pregnant women with gestational diabetes 1.47 times more often than unvaccinated pregnant women (12.2% vs. 8.3%; $p = 0.02$).

**7.7.5 Male Fertility Analysis.** In Gat et al.'s small study of 37 sperm donors, researchers found a 15.4% reduction (95% CI −25.5% to −3.9%, $p = 0.01$) in sperm concentration and a 22.1% reduction (95% CI −35% to −6.6%, $p = 0.007$) in the total number of viable sperm in the period from 75 to 125 days after vaccination with the Pfizer BNT162b2 vaccine [338]. Both sperm concentration and total motile sperm count remained reduced when measured after 145 days, with decreases of 15.9% (95% CI −30.3% to 1.7%) and 19.4% (95% CI −35.4% to 0.6%), respectively, compared to baseline values. However, these results were not statistically significant due to high variability in measurement and small sample size. The results to not support the authors' claim that recovery of semen parameters was evident.

**7.7.6 Summary.** This collection of surveillance, survey, and retrospective cohort analyses following the rollout of these untested products demonstrate concerning trends of menstrual irregularities, adverse pregnancy outcomes, fetal abnormalities, and impaired male fertility. These reports only scratch the surface of short- and long-term reproductive effects yet unmeasured and unrecorded in the peer-reviewed literature.

## 7.8 Conclusion

While large-scale epidemiological studies that are free from financial conflicts of interest and that directly compare health outcomes between vaccinated and unvaccinated groups are scarce, the available evidence begins to piece together a concerning picture of illness, disability, and death following mRNA COVID-19 vaccination. And these are primarily only the short-term effects, observed within days to six weeks post-injection. It may take months, years, and decades for the damage of these toxic biological agents to manifest in chronic cardiac, thrombotic,

neurological, immune, reproductive, and other organ dysfunction. Despite dozens of peer-reviewed papers already demonstrating significant harms of mRNA COVID-19 vaccines, the CDC persists in asserting that these injections are safe [339]. As of December 2022, the CDC recommends COVID-19 vaccines "for everyone ages 6 months and older, and boosters for everyone 5 years and older, if eligible" (ibid.). Regardless of whether or not the government health agencies choose to acknowledge it, epidemiological research will continue to help elucidate the destructive effects these mRNA injections have on the health of men, women, and children.

# 8. AIDS & HIV: The Blueprint for the Perversion and Subversion of Medical Science

David Rasnick, Ph.D.

*If ever there was a rush to judgment with its predictable disastrous results it has been the HIV/AIDS hypothesis and its aftermath. Announced at a press conference prior to the publication of any scientific proof, complicated and confused by early legal arguments concerning theft of the "French" virus by American researchers, the continuing inability of a worldwide scientific effort to muster clear proof for causality of AIDS by HIV, the inability—after 10-plus years and billions of dollars—to generate any progress in prevention or therapy, and amid growing controversy about effectiveness of drugs like AZT to have any benefit, the HIV/AIDS hypothesis remains simply that: a theory with erratic correlation, but no proof of causality, between HIV and AIDS. I say "erratic," because of the many HIV-positive cases with no AIDS and of the many AIDS cases with no HIV, and also because the circular definition of AIDS (no HIV = no AIDS) makes any correlation meaningless to begin with (AIDS patients without HIV are not officially listed by the CDC as having AIDS).*

*From the Preface by Professor Dick Strohman, UC Berkeley, to the book* Infectious AIDS: Have We Been Misled? *by Professor Peter Duesberg [340]*

The AIDS scare of the 1980s and 1990s is important to the story of COVID-19 because that's when the global governmental-institutional-pharmaceutical infrastructure which rules the world today was put in place. AIDS was my initial contact with corrosive, dogmatic science. In the 1980s, I witnessed the abrupt end to free and open scientific

inquiry into AIDS at a crucial point when expansive, creative thinking would have been essential. I lost friends and colleagues when I raised questions about the presumed contagiousness of AIDS.

President Reagan's first term in office coincided with the first four years of AIDS. His administration had been silent on AIDS until April 23, 1984, when a press conference was called in order to forestall the Democrats turning AIDS into a campaign issue. Margaret Heckler, Secretary of the Department of Health and Human Services (HHS), announced that Dr. Robert Gallo of the National Cancer Institute had discovered a retrovirus, later called HIV, that was the probable cause of AIDS. (The very next day, the word "probable" was dropped.) The Reagan Administration promised a vaccine in 2 years. Six administrations on, we're still waiting!

Gallo's discovery of the viral cause of AIDS came as a complete surprise to every interested scientist in the world. Not a single word about it had appeared in any scientific or medical journal, nor had the idea been discussed at any scientific meetings prior to this press conference. Anthony Fauci, the newly appointed Director of the National Institute of Allergy and Infectious Diseases (NIAID), used the AIDS scare to perfect "science by press release." The usurping of scientific scrutiny and debate by Fauci quickly led to the establishment of a fraudulent AIDS scenario, which remains dogma to this day:

- AIDS is contagious
- AIDS is sexually transmitted
- AIDS is caused by HIV
- AIDS originated in Africa
- AIDS is inevitably fatal

However, not one of these assertions is true [340, 341]!

A scientific theory is always subject to change—at any time, "something better" might take its place. It's the job of the scientist to keep looking for that "something better" and recognize it when it appears. An individual or group proposing a superior theory, a better understanding of reality, usually welcomes an honest challenge by other scientists. Interrogating a truly superior theory only makes it better, and in the process it reveals the deficiencies of competing theories. At least, this is how scientific progress is supposed to work; but unfortunately, institutional science has largely destroyed this ideal.

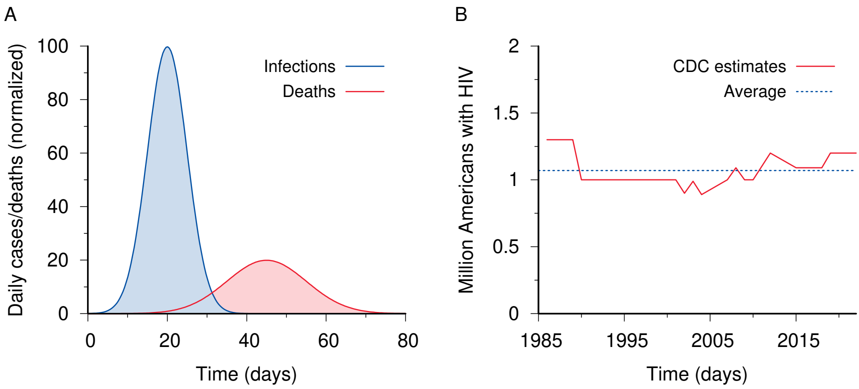



**Figure 8.1** Farr's law of acute contagious disease, and long-term trend of HIV infections in the U.S. population. **A:** Infections rise as a novel germ spreads within a non-immune population, but the number soon recedes as the number of not yet infected susceptible individuals decreases. Deaths follow a similar time course, but at lower numbers and with a certain delay which depend on the natural course of the disease. **B:** Time course of HIV infections in the U.S. population according to CDC estimates [342].

The conjoining of government, big business and academe which President Eisenhower warned about in 1961 now rules the world. This supranational network protects the status quo by silencing minority opinions and voices through the imposition of dogma which cannot be questioned, corrected, or retracted. I have witnessed the institutional despotism that punishes, persecutes, torments and silences anyone who challenges scientific and especially medical dogma. The control of information and its orchestrated dissemination is so widespread and pervasive that it is impossible for people to know what's really going on—what's true and what's not.

## 8.1 AIDS does not behave like a novel contagious disease

AIDS does not behave like a contagious disease [340, 341]. Contagious diseases by and large do not discriminate between the sexes or races. Somehow, AIDS does. Furthermore, novel contagious diseases spread very fast throughout the population, reach a peak, and then decline rapidly, following a bell-shaped curve over a period of weeks to months (see Figure 8.1A). This is known as Farr's Law of Contagious Disease [340, p. 266].

An infection with HIV, we're told, takes years or even more than a decade to cause clinical AIDS [340, p. 156, p. 297]. The CDC has been claiming around 50,000 new HIV infections annually in the USA [343, 344]. However, between 1986 and 2022—a period of 37 years!—there has been roughly a constant 1 million Americans "living with HIV" (see Figure 8.1B). That could only happen if an equal number of HIV-positive Americans died each year.

## 8.2 AIDS and drug abuse

The two clinical conditions which initially were considered to define AIDS were immune suppression and Kaposi's sarcoma. For at least two years prior to 1984, the CDC was aware that the occurrence of these two diseases in gay men was strongly associated with the gay lifestyle, in particular the heavy use of recreational drugs, especially poppers [345, 346]. Poppers were inhaled by "fast-track" male homosexuals as bathhouse aphrodisiacs and muscle relaxants to facilitate anal intercourse. Poppers—chemically known as alkyl nitrites—are very chemically reactive and strong carcinogens. As an organic chemist myself, I would not open a bottle of that stuff outside of a chemical fume hood.

Gay AIDS activist, writer and journalist John Lauritsen died on March 5, 2022. In the early 1980s he began circulating warnings in the gay community about the dangers of recreational drugs. On February 14, 1985, Lauritsen published in the Philadelphia Gay News his first article on AIDS: *"CDC's Tables Obscure AIDS-Drugs Connection."* He showed that the CDC was hiding the association between poppers and Kaposi's sarcoma. In 1993, Lauritsen published his book *The AIDS war: propaganda, profiteering and genocide from the medical-industrial complex* [347], a collection of his major writings on AIDS going back to 1985, which also includes the above article.

Published studies on gay men with AIDS indicate that many of them had something in common besides sexual orientation. They were drug abusers—not necessarily of intravenous drugs, but nonetheless regular and generally heavy users of many different unhealthful chemical substances, including quaaludes (barbiturate-like sedatives), cocaine, nitrite inhalants (poppers), ethyl chloride, amphetamines, tuinal, barbiturates, uppers, downers, etc. Lauritsen did his best to alert the gay community to the dangers of these drugs, but as he soon discovered,

the widespread hostility to his message meant that he could publish only in the gay press, and then only in a small subset of that.

## 8.3 Peter Duesberg's scientific critique of the HIV/AIDS hypothesis

In 1987, Lauritsen received scientific support for his skepticism of the HIV/AIDS hypothesis. Professor Peter Duesberg, virologist at the University of California Berkeley and member of the National Academy of Sciences, published an article commissioned by Peter Magee, editor of the prestigious journal *Cancer Research*, in which he concluded that HIV was not sufficient to cause AIDS. Lauritsen interviewed Duesberg for the July 6, 1987, edition of the *New York Native*. Duesberg explained that viruses such as HIV typically do not kill cells and, even if HIV did kill cells, it infects so few cells that their death could have no serious effect on a person's health.

In a 1994 review of Lauritsen's book *The AIDS War*, Mike Chappelle said [348]:

> *One might expect that the conclusions of a high-ranking scientist such as Duesberg—that HIV cannot cause AIDS (and variations on this theme by a growing number of other scientists)—should have made the headlines by now. However, with few exceptions (notably the London Sunday Times), they have not. Nevertheless, the breaking of the link between HIV and AIDS eventually enabled Lauritsen to arrive at his remarkable conclusion that AIDS does not exist.*

During the first 10-years of AIDS, 9 out of 10 cases in the United States were men: primarily male homosexuals and heterosexual intravenous drug users. Even after the CDC added cervical cancer to the list of diseases that could define AIDS in 1993, American women still obstinately refused to get AIDS. For example, in 1997—the last year the CDC reported statistics on AIDS-defining diseases—cervical cancer accounted for only 1% of all AIDS cases [349].

AIDS is clearly not contagious. And as incredible as this may sound, there has not been a single scientific study designed or conducted to determine whether or not AIDS—or even HIV—is sexually transmitted. In the absence of proof, the sexual transmission of AIDS and HIV has become axiomatic "truth."

## 8.4 HIV is not sexually transmitted

The literature on retroviruses, the family of viruses to which HIV belongs, goes back over a hundred years [340, 341]. Every person and animal on the planet carries 50 to 100 or even a thousand dormant retroviruses in their genomes [350]. It is estimated that up to 8% of the human genome is made up of retroviruses [351]. Over 3,000 different retroviruses have been cataloged and not one to date has been demonstrated to cause disease in humans.

For at least 70 years, scientists have known that retroviruses do not kill the cells they infect and are not sexually transmitted [340]. Retroviruses are so not-sexually transmissible that you can mix different strains of rodents with their unique spectrum of retroviruses and they never transmit them to their sex partners from a different strain. This is also true for humans, apes, monkeys, and cats.

The experimental versions of HIV used in laboratory animals have never been shown to be sexually transmitted to virus-free sex partners. The world's best controlled human study that attempted to measure the efficiency of heterosexual transmission of HIV was conducted by Nancy Padian and her colleagues [352]. The most striking result of this ten-year study was that none of the HIV-negative sex partners became HIV-positive from years of unprotected sexual intercourse with their HIV-positive partners. I repeat, not one HIV-negative sex partner became positive during the 10-year study. Thus, the observed transmission efficiency was ZERO!

However, to avoid reporting zero sexual transmission of HIV, Padian and colleagues assumed that the HIV-positive sex partners in their study must have become positive through sexual intercourse *before* entering the study. Using that assumption, they estimated that an HIV-negative woman would need to have sexual intercourse 1,000 times with HIV-positive men before becoming HIV-positive herself. Even more astoundingly, they estimated that HIV-negative heterosexual men would need 8,000 sexual contacts before becoming HIV-positive. Virtually identical figures have been reported by others [350, 353, 354].

Given these figures, the CDC's estimate that "one million Americans are living with HIV" raises an enormous problem for the assumed sexual transmission of HIV. Since there were around 280 million men and women in the USA during the AIDS scare, on average an HIV-negative

woman would require 140,000 episodes of random sexual intercourse in order to become HIV-positive, and a man fully eight times that number.

Such absurdly high numbers of sexual encounters are out of reach even for prostitutes. Against this background, it makes a certain amount of sense that sex with a prostitute is not even listed as a risk category for AIDS by the CDC. According to Root-Bernstein [355], "the number of American and European heterosexuals who have had sexual relations with a prostitute, who have no other admitted risk factors (such as drug abuse), and who have subsequently developed antibody to HIV can be counted on the fingers of one hand." Non-drug abusing American prostitutes have no higher risk to contract AIDS than other women [356]. The same is true for prostitutes in Germany, Zurich, Vienna, London, Paris, Pardenone (Italy), and Athens [357–361].

## 8.5 Kary Mullis' quest for evidence that HIV causes AIDS

In 1988, Kary Mullis, winner of the 1993 Nobel Prize in chemistry for inventing the polymerase chain reaction (PCR), needed a literature reference to support the statement he had just written: "HIV is the probable cause of AIDS." He simply wanted to cite the person who had demonstrated that HIV was indeed "the probable cause of AIDS." He soon learned, to his dismay, that the individuals—who it seemed would surely be candidates for a Nobel Prize—had no name. In 1994, Mullis had the opportunity to ask Luc Montagnier, the discoverer of HIV, whom to cite. But even Montagnier did not know. In 2000, Montagnier himself came to reject the central feature of AIDS dogma, namely, that HIV causes AIDS [362].[1]

Mullis became an outspoken critic of Anthony Fauci's mishandling of AIDS and of those advocating the use of PCR-testing to detect viruses and diagnose infectious diseases. In an interview in the London Sunday Times, Mullis said [363]:

> *I can't find a single virologist who will give me references which show that HIV is the probable cause of AIDS. On an issue as important as this, there should be a set of scientific documents somewhere, research papers written by people who are accessible, demonstrating this. But they are not available. If you ask a*

[1] Note that Montagnier was awarded the 2008 Nobel Prize for discovering HIV—not for proving that HIV causes AIDS.

> *virologist for that information, you don't get an answer, you get fury.*

Mullis died August 7, 2019, just before PCR testing launched the global COVID-19 fraud.

In April 2020, Montagnier concluded that SARS-CoV-2 had been created in a lab because genetic sequences of HIV had been inserted into the gene encoding the spike protein [364]. Montagnier died on February 8, 2022, just 8 months after criticizing the global push to "vaccinate" against COVID-19 [365].

## 8.6 The crucifixion of a dissident

Duesberg's assault on the causative role of HIV went completely unchallenged in the scientific literature—a tacit admission among scientists that his arguments were, at the very least, compelling and most likely irrefutable. As the most credentialed, persistent and effective critic of AIDS dogma, Peter Duesberg was at the top of Anthony Fauci's hit list. The U.S. Department of Health and Human Services (HHS) decided to "contain" Duesberg's ideas so that the public would not learn about them. On April 28, 1987, two months after Duesberg's *Cancer Research* paper had appeared, Chuck Kline of the Office of the Secretary of HHS sent out a "Media Alert" [366]:

> *An NCI [National Cancer Institute] grantee scientist, Dr. Peter Duesberg of California/Berkeley, has published a paper in a scientific journal which concludes that the HTLV-III/HIV virus identified by Dr. Gallo and Dr. Montagnier is not the cause of AIDS and that the disease is caused by "a still unidentified agent" which may not even be a virus.*
>
> *Inexplicably, the paper was published in the March 1 addition [sic] of Cancer Research, and gives a non-specific credit to Dr. Robert Gallo and others, but nobody within the Department or the news media seems to have been aware of it until it was disclosed Monday, 4/27, by a gay publication in New York City.*
>
> *Dr. Duesberg has been an NCI grantee doing research in retroviruses and oncogenes for 17 years and is highly regarded. He is the recipient of an "outstanding researcher" award from the Department. The article apparently went through the normal pre-publication process and should have been flagged at NIH.*

*Failing that, it should have caused a splash on publication nearly two months ago.*

*Playwright, gay activist and Department critic Larry Kramer is currently bringing it to the attention of the media, but it really hasn't taken off yet. I know for instance he has talked to Tom Brokaw about it. There has been one call to CDC from Newsday and none to the press office so far.*

*This obviously has the potential to raise a lot of controversy (if this isn't the virus, how do we know the blood supply is safe? How do we know anything about transmission? How could you all be so stupid and why should we ever believe you again?) and we need to be prepared to respond. I have already asked NIH public affairs to start digging into this.*

*Chuck Kline*

*cc:*

*The Secretary*
*The Under Secretary*
*Chief of Staff*
*Assistant Secretary for Health*
*Surgeon General*
*Assistant Secretary of Public Affairs*
*The White House*

Since World War II—but especially in recent decades—the stifling of debate and the persecution of dissenters has become entrenched in virtually every major field of science in the United States. It is particularly virulent in the so-called biomedical sciences.

For more than three decades, the National Institutes of Health (NIH), the National Cancer Institute (NCI), and Centers for Disease Control (CDC) have employed every weapon available to silence and punish Professor Duesberg for his steadfast refusal to recant, or at least remain silent. Prior to questioning HIV, Duesberg had been continually funded by the NIH as a cancer researcher in high standing, and was even awarded the coveted "Outstanding Investigator" grant.

With jaw-dropping swiftness, Duesberg lost all government funding grants following the appearance of his 1987 invited paper in *Cancer Research* questioning AIDS dogma [367]. He has not had a new graduate student since the early 1990s. Some premier science journals have

stopped publishing his work. Because of tenure, Duesberg can't be fired. For this reason, the University of California at Berkeley has marginalized, humiliated, and punished Duesberg continually, hoping he would leave voluntarily.

## 8.7 AIDS in Africa

Most people are not aware that the CDC—and the World Health Organization, which follows its lead—defined two very different AIDS epidemics. There is one definition for Americans, Europeans, and other wealthy nations, and a very different definition for Africans, Asians, Latin Americans, etc. You get the picture. The reason for this peculiar situation is that AIDS is completely different depending on where you live. So different in fact that the Reagan Administration urged the WHO to come up with a definition of AIDS in the "Third World." In 1985, at a conference in Bangui, the capital of the Central African Republic, AIDS in Africa was defined as a grab bag of symptoms including fever, diarrhea, persistent cough, and weight-loss [368]. To this list, tuberculosis was added in the mid 1990s. These long-recognized diseases of poverty and malnutrition remain the basis for making a diagnosis of AIDS in Africa to this day. Amazingly, HIV was not even part of the definition! Using the Bangui definition, it could be said that African AIDS has been around for hundreds of years.

In George Orwell's iconic year 1984, the cover of Newsweek asked: "Can Black Africa Be Saved?" This was only months after the Reagan Administration had told the world that AIDS had started in Africa and was caused by a virus. Two years later the piece "Africa in the Plague Years" appeared in the same journal. The authors informed us: "Nowhere is the disease more rampant than in the Rakai region of south-west Uganda, where 30% of the people are estimated [not determined] to be seropositive [for HIV] [369]."

In 1995, the World Health Organisation poured fuel on the fire declaring: "by mid-1991 an estimated 1.5 million Ugandans, or about 9% of the general population and 20% of the sexually active population, had HIV infection" [370]. Similar reports were repeatedly published over the next several years, prophesying that as much as 30% of the population was doomed to premature death, with dire consequences for families and society as a whole. The predictions announced the practically inevitable collapse of the country in which the entire worldwide epidemic had supposedly originated.

Today one reads little about AIDS in Uganda, because all of these prophesies have proved false. In its 2002 census, the Uganda Bureau of Statistics [371] reported that

> *Uganda's Population grew at an average annual rate of 3.3% between 1991 and 2002. The high rate of population growth is mainly due to the persistently high fertility levels (about seven children per woman) that have been observed for the past four decades. ... There has been a declining trend in Infant Mortality Rate from 422 per 1000 as of the 1991 Census ... to 83 per 1000 live births in 2002.*

The census report makes clear that Uganda's population growth rate, which had been as high as 2.5% between 1980 and 1991, had indeed *further increased* in the subsequent decade. Uganda's population growth rate is currently among the highest in the world. Nevertheless, the popular media continued to inform us that the whole of Sub-Saharan Africa had suffered massive devastation and depopulation as a result of more than three decades of AIDS. Notwithstanding these claims, the statistics make it extremely difficult to find evidence of an African AIDS catastrophe on a scale that some have compared to the European plague of the Middle Ages.

By 2001, Africa had reportedly generated a cumulative total of 1,093,522 AIDS cases [372]. But during this period—between 1980 and 2000—the population of Sub-Saharan Africa had grown from 378 million to 652 million, corresponding to an annual growth rate of 3.6%! Of course, against this background, a possible, above-normal loss of one million lives to AIDS would be statistically hard to verify, for two reasons:

1. the loss would be dwarfed by the overwhelming simultaneous gain of 274 million people—the equivalent of the entire population of the USA in 1999;
2. the diseases which according to the Bangui criteria define African AIDS are indistinguishable from conventional African morbidity and mortality [370].

As of May 2019, the population of Sub-Saharan Africa had grown to 1.08 billion. Compared to 1980, that is a gain of 700 million people, or *twice* the population of the United States! The population of Sub-

Saharan Africa grew by an explosive 2.8 times since the AIDS epidemic supposedly began in Africa.

The explosive population growth of Sub-Saharan Africa and the many epidemiological and clinical differences between African AIDS and its American/European namesake cast doubt on the existence of an African AIDS epidemic. Indeed, all available data are compatible with a perennial African epidemic of poverty-associated infectious diseases which simply has been given the new name of "AIDS."

## 8.8 Thabo Mbeki's ill-fated attempt to get at the truth about AIDS

Aware of this history and faced with the disturbing fact that his country's "scientists don't read," South African President Thabo Mbeki was compelled in 1999 to ask: why is AIDS in Africa so vastly different from AIDS in North America and Western Europe? Why does AIDS remain restricted to the same at-risk groups in which it was originally observed? To get answers to these and other questions, he set up the Presidential AIDS Advisory Panel in 2000.

In order to gain a full understanding of AIDS, a decision was taken to invite an international panel of experts to South Africa and provide a platform for them to deliberate on the issues pertaining to the subject. The results of these deliberations would be used to inform and advise the government on the most appropriate course of action to follow in dealing with AIDS. This decision was endorsed by the Cabinet of the South African government in April 2000. A world-wide search took place to identify eminent specialists in the fields of AIDS and HIV, ranging in scope from basic scientists, physicians, historians, economists to public health professionals and policy makers. Furthermore, it was decided that persons living with AIDS, as well as lay persons would be invited to serve on the panel.

South Africa's recent experience of coming to terms with its history of Apartheid had taught Mbeki the necessity of including dissenting voices. One third of Mbeki's AIDS Advisory Panel comprised scientists and doctors from around the world who questioned AIDS dogma. The two meetings of the advisory panel resulted in an extensive written report [373].

The inclusion of dissident scientists in this advisory panel did, however, not sit well with some representatives of the AIDS orthodoxy and with the U.S. government. Accompanying a sign with the words "One Bullet, One Dissident," the head of *Médecins sans Frontières* led

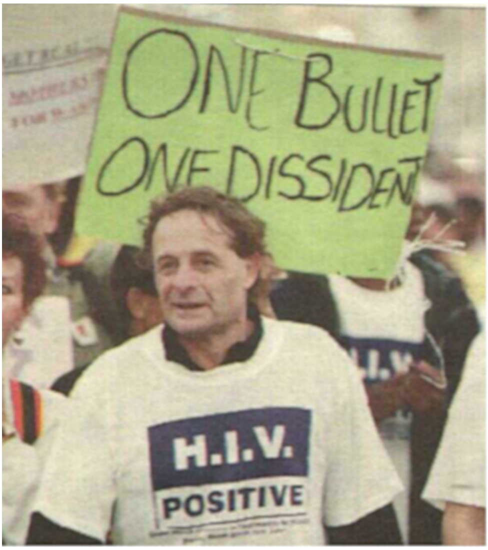



**Figure 8.2** Angry HIV-positive people march through Durban, South Africa, between July 14 to 20, 2000 to protest against scientists who dare to question whether AIDS is caused by HIV. Mail & Guardian, vol 16, no 28, page 8.

a march through the South African city of Durban, protesting against those scientists on the AIDS Advisory Panel who wanted answers to the same questions about AIDS that Mbeki had asked (Figure 8.2). Others advocated that the dissidents be jailed, or that the U.S. constitution be changed to prevent them from speaking.

While these protests and efforts to silence the dissidents were in progress, observers on Mbeki's AIDS Advisory Panel noted that [373, p. 45]

> *The deliberations of the panel were at all times bedevilled by the absence of accurate and reliable data and statistics on the magnitude of the AIDS problem or even HIV prevalence in South Africa. Repeated requests for such data and statistics failed to result in the provision of such data by either South African panelists or the officials of the Department of Health.*

While mainstream AIDS researchers agreed that South Africa has the best statistics in Africa, these same experts failed to point out that from 1994 to 2001, South Africa recorded a constant annual population growth rate of about 2%. All cause mortality did increase

during the same time interval, but only a small fraction of all deaths were attributed to HIV according to government statistics [374].

In May 2000, an open forum was convened in Pretoria, the capital of South Africa. The goal was to discuss the central issues of AIDS in Africa and address the government's specific questions, so as to come up with the best evidence available to help the government decide what AIDS policy it should pursue. The government had invited internationally recognized AIDS authorities, who accounted for two-thirds of the panel, but also a "Who's Who" of international critics, who formed the remaining one-third of the participants.

From day one, the AIDS establishment did everything it could to torpedo President Mbeki's AIDS Advisory Panel. Since the idea that AIDS is contagious and caused by HIV had originated with the U.S. government's Department of Health and Human Services, the Clinton administration had to discredit Mbeki's probing of AIDS dogma and prevent an open public debate about the causes of AIDS. But to simply reject Mbeki's invitation was just too politically untenable for the United States and the other governments that follow its lead. After all, world leaders at the time were committed to supporting South Africa's new democracy that had recently emerged from the oppression of apartheid. To keep from embarrassing the government of South Africa, the United States reluctantly sent a contingent of AIDS authorities. AIDS czar Anthony Fauci was conspicuously absent.

The attempt to reconcile the irreconcilable doomed Mbeki's effort. It was clear from the start that the mainstream panelists had agreed among themselves, or were instructed beforehand, not to participate in any of the discussions in good faith. An overt provocation happened at the first meeting soon after the invited panelists had been seated. Three African-American "physicians"—carrying themselves like FBI agents, wearing dark suites and grim expressions—were added to the panel at the last minute. That they were all Blacks escaped no one. In contrast to the invited panelists, there were no name-plates to identify the newcomers. A few of the African delegates were irate with the sudden appearance of the strangers. The meeting was about to come unhinged before it started.

A rumor quickly spread that President Clinton had asked Mbeki to include the unnamed panelists. Professor Mhlongo asked the panel and the moderator if the rumor was true but received no answer. Eventually, a woman from Mbeki's office appeared and said Clinton

had indeed asked that these people join. Other than maintaining a menacing presence as Clinton's eyes and ears, I don't recall the strangers contributing anything at all to the meeting.

When the meeting finally got underway, the mainstream panelists flat-out refused to participate and did everything they could to derail the conference. Peter Duesberg was about to give the first presentation when somebody loudly objected. The not so neutral moderator—Stephen Owen, a Canadian law professor—acquiesced to the mainstream's demand that no data be presented, demolishing even the pretense of a scientific exchange. This was noted in the official report of the Panel proceedings [373, p. 108]:

> *The nature and format of the deliberations of the panel could not allow the in-depth scientific argumentation that is necessary to resolve many of the differences over scientific issues of a fundamental nature.*

The second meeting of the Panel that took place in Johannesburg conveyed a decidedly more professional appearance than the first. High-level South African officials expressed the government's anger and frustration with the mainstream's stonewalling during the first meeting and especially their boycotting of the internet discussions that had been designed to come up with the agenda for the second meeting. The government discovered that the mainstreamers had set up their own internet discussions, urging other members of Mbeki's panel not to participate. Weaponizing their AIDS dogma, the mainstreamers secretly engaged in an international email campaign, which led to the Durban Declaration that was designed to discredit and neutralize Mbeki's AIDS Advisory Panel.

The Durban Declaration was released just before the second meeting of the Panel in June. A few days later, it was published in the journal Nature [375]. The purpose of these 18 paragraphs of text was to stop any criticism of AIDS dogma once and for all. A number of the orthodox members on the AIDS Panel were signatories. Infuriated, the South African government lifted the prohibition on presenting data and tried to shame the orthodox panelists into engaging in a real scientific debate this time around. However, it was too little, too late.

The South African Broadcasting Corporation (SABC) had received permission from the government to provide live coverage of the AIDS Panel. However, the mainstream members refused to participate if

that was allowed. So, the government relented and SABC was excluded. Nevertheless, the entire proceedings of the Panel were video-recorded by the government. The Panel was told the video and transcripts would be made available to the world at some point. This, of course, has not happened. The people of South Africa and the world have the right to see those videos. Releasing the video record of the mainstream's stonewalling and behavior would be at least as explosive, embarrassing, and damaging to the United States as the Nixon Watergate tapes.

Advocates of AIDS dogma invariably resort to the historically effective practice of verbal abuse. Among other things, dissidents are accused of being flat-earthers, denialists, murderers, psychopaths, unethical, and immoral with African blood dripping from their fingers. If any of that were true, President Mbeki's AIDS Advisory Panel should have provided the perfect opportunity for the orthodoxy to show the government of South Africa and people of the world convincing evidence that AIDS is in fact contagious, sexually transmitted, and caused by a virus called HIV. They could have presented the government of South Africa with the evidence that the toxic anti-HIV drugs actually do more good than harm, as Mbeki had specifically requested. It's difficult to see how that would be bad—right?

## 8.9 Some evidence to challenge the AIDS orthodoxy

Even more important from the mainstream perspective, the meetings in South Africa should have offered the perfect setting for the orthodoxy to publicly obliterate the dissidents' position that AIDS is not contagious, not sexually transmitted, and not caused by HIV. Instead, they authored the Durban Declaration. Except for the dissidents in attendance, I can't recall anyone anywhere admonishing the orthodoxy for failing to use the AIDS Panel to publicly confront and demolish the dissidents with solid scientific evidence. Here are some examples of the evidence which the mainstream members of the panel did not want to examine in public.

If HIV were indeed sexually transmitted, then its prevalence should resemble that of other sexually transmitted diseases. However, Figure 8.3 shows that there is a *negative* correlation between sexually transmitted syphilis and the prevalence of HIV among pregnant women in the South African provinces [369, 376, 377]. Similar results have been reported for Uganda and Thailand. There is also an anti-correlation

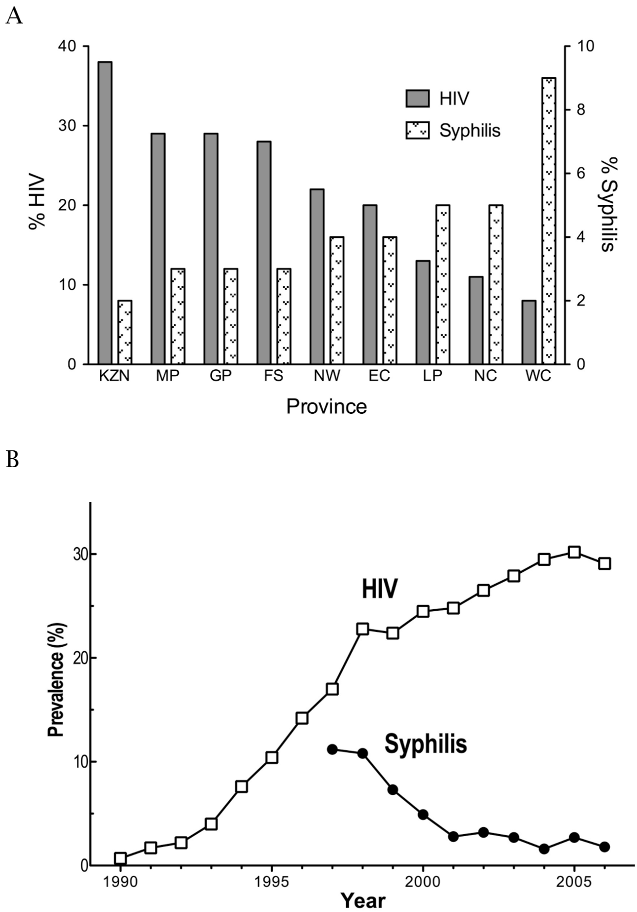



**Figure 8.3** Negative correlation between HIV and syphilis prevalence in South Africa [376]. **A:** Prevalence of HIV and syphilis by province among antenatal clinic attendees in 2000. Provinces: KwaZulu-Natal (KZN), Mpumalanga (MP), Gauteng (GP), Free State (FS), North West (NW), Eastern Cape (EC), Limpopo (LP), Northern Cape (NC), Western Cape (WC). **B:** National HIV and syphilis prevalence trends among antenatal clinic attendees in South Africa 4. Data for syphilis prior to 1997 were unavailable.

between syphilis and HIV prevalence over time [376]. Again, similar results have been reported for Uganda and Thailand.

Notwithstanding this history and the complete absence of scientific proof that AIDS is contagious, sexually transmitted, and depopulating Africa, the CDC, Fauci's NIAID, the WHO etc., continue to assert that HIV causes AIDS [374].

The COVID-19 fraud is the AIDS scam writ large. There is wholesale silencing of any and all critics, regardless of stature. Families and friendships are splitting apart over questioning government dogma on COVID-19. For a host of reasons and across a wide spectrum of livelihoods, professions and careers many millions of people have lost jobs. We are in the middle of a global totalitarian takeover and things are going to get much worse in the months ahead.

# 9. Summary and conclusions

The main purpose of this book was to help solve the following question:

> *What does the COVID-19 mRNA vaccine experience tell us about the safety of future mRNA vaccines?*

Let us now try to answer it, in light of what we have learned after surveying the evidence.

## 9.1 The key mechanism of mRNA vaccine toxicity

We have encountered at least three potential pathogenetic mechanisms that might account for the toxicity observed with the mRNA vaccines against COVID-19, namely:

1. the chemical toxicity of lipid nanoparticles,
2. direct toxicity of the spike protein, whose expression is induced by the vaccines, and
3. the destructive effects of the immune response to the spike protein.

Of these, we consider the third one the most important one, for the following reasons:

1. it follows from the theoretical considerations that were presented in Chapter 3, and
2. it accounts for the histopathological findings of intense inflammation and infiltration by immune cells, particularly lymphocytes, which are observed near foci of spike protein expression, as documented in Chapter 4.

A third consideration that favors this mechanism is the increased adverse event incidence and severity after repeated vaccine injection, which is documented in Chapter 7. In contrast, the chemical toxicity of cationic lipids is independent of the specific immune system, and we would therefore expect it to be of similar intensity after each injection.

Moreover, the adenovirus-based vaccines produced by AstraZeneca and Johnson & Johnson have fairly similar profiles of adverse events to the mRNA vaccines, even though they do not contain any cationic lipids. The direct toxicity of the spike protein should be inhibited by specific antibodies; therefore, its intensity should diminish rather than increase after repeat injections.

We thus conclude that overall the immune-mediated attack on cells that express the antigen encoded by the mRNA vaccine is the leading pathogenetic mechanism. This does not mean, however, that the other two mechanisms of harm should be discounted. Direct spike protein effects may well contribute to early adverse events after the first injection, particularly in those without any preexisting immunity to the virus. The toxicity of cationic lipids cannot be dismissed either, for the following reasons:

1. almost no safety studies were conducted on these substances during the dysfunctional approval processes of the COVID-19 vaccines, but the rudimentary ones which were performed gave clear indications of toxicity (see Section 6.1);
2. the induction of reactive oxygen species (ROS) by cationic lipids (see Section 5.3.3) will cause DNA damage. This damage will stay behind even after the lipids themselves have been eliminated, which means that toxicity will be cumulative;
3. since cationic lipids are a necessary ingredient of all mRNA vaccines (see Section 5.1.4), their toxicity will accumulate across all doses of all mRNA vaccines, rather than just across all doses of a single such vaccine.

## 9.2 The immunological mechanism of harm is completely general

We had seen in Chapters 2 and 3 that all that is needed to trigger an immune response is the presence of a foreign antigen, in combination with some non-specific inflammatory stimulus; the biological activity, toxic or otherwise, of the antigenic protein itself is unimportant in this context. Every future mRNA vaccine will induce our cells to produce its own specific antigen, related to the particular microbe it targets. We must therefore expect each such vaccine to induce immunological damage on a similar scale as we have witnessed with those directed against COVID-19.

## 9.3 Could a return to good manufacturing practices abolish the toxicity of the mRNA vaccines?

A rather startling observation pertaining to the COVID-19 mRNA vaccines is just how heavily they are contaminated. Well-documented contaminations include plasmid DNA and metallic particles (Section 5.4.1). Moreover, the extraordinarily large variation in the number of adverse events reported for different batches (Section 5.4.2) clearly indicates highly inconsistent manufacturing standards. If these contaminants were removed, and if consistent standards were observed, might this remove the threat of mRNA vaccine toxicity?

There are two considerations. The first is that the observed key mechanism of harm results from the vaccines working as intended: the vaccines induce the expression of the antigen in our body cells, and the immune response to the antigen kills those cells. We therefore have to expect that greater and more consistent product quality will increase rather than decrease the number of casualties.

The second consideration concerns the DNA contamination. As pointed out in Section 6.3, the risks posed by plasmid DNA contained in the vaccines are twofold: firstly, damage to the genome, potentially leading to cancer and leukemia, and secondly the prolonged expression of the antigen, with extended duration and increased severity of the immune response to it. Thus, if the effective removal of DNA from the vaccines could be ensured, this should indeed mitigate their toxicity. However, it is likely that in the initial days after vaccine injection the expression of the antigen is mainly driven by the mRNA itself. Many severe adverse events tend to become manifest within days of the injection, for example myocarditis, stroke, and heart attacks (see Chapter 7). It is therefore unlikely that avoiding DNA contamination will put an end to mRNA vaccine toxicity or reduce it to levels deemed "acceptable" with conventional vaccines.

## 9.4 If mRNA vaccines are inherently dangerous, why are they urged and even forced on us?

At this point in history, there is no need to beat around the bush. It is no longer possible to construe the actions of the authorities as "honest mistakes." Too much has occurred that points unequivocally to a sinister agenda behind the gene-based COVID-19 vaccines. The rushed approval without necessity, the outright threats and the coercion, the

systematic censorship of honest science, and the suppression of the truth about the numerous killed or severely injured vaccine victims have all gone on for far too long to permit of any doubts as to intent and purpose. Our governments and the national and international administrative bodies are waging an undeclared war on all of us. As David Rasnick points out in Chapter 8, this war has been going on for decades, and we must expect it to continue and to escalate.

## 9.5 What can we do?

First and foremost, we must accept that we are indeed in our governments' cross hairs. Instead of relying on their treacherous and malevolent guidance, we must therefore watch out for ourselves and our loved ones—do our own research and seek out honest health advice wherever it may be found, be it inside or outside the established venues of science and of medicine. We hope that with this book we have helped you to take one step on that journey.

# Afterword

Catherine Austin Fitts, President, The Solari Report

> I call heaven and earth to record this day against you,
> that I have set before you life and death, blessing and cursing:
> therefore choose life, that both thou and thy seed may live.
>
> Deuteronomy 30:19

There are several things to consider regarding what you have learned reading *mRNA Vaccine Toxicity* by the Doctors for COVID Ethics.

The certainty that mRNA technology kills and maims—and that this was known by those who made and released the COVID-19 vaccinations—is priceless intelligence. Having this knowledge gives you the power to protect yourself and the people you love. Your doing so is of the utmost importance to the network of doctors, scientists, and researchers who have worked to understand and communicate these dangers.

Many of the doctors and scientists who have helped expose the lethality of mRNA technology over the last three years had little or no expectation of what they would find when they began their investigations. They were people with prominent positions or retired from the same. They had confidence in the establishment—in the scientific establishment, in the medical establishment, in the academic institutions that support science and medicine, and in government and its regulatory agencies. They also had busy lives—and while understanding the dangers of growing corruption, they did not realize that a mass atrocity implemented by such means across the globe, including in the Western world, was possible. Yet upon discovering the facts, they faced what needed to be faced and persevered.

Some of them have now lost positions and titles. They have lost income and benefit packages. They have worked without compensation for countless hours. They have been targeted by media slander and disinformation. Some have been the target of baseless investigations, lawsuits, and prosecution. Some have lost medical licenses. Some have lost homes, families, and friends. I believe that some have been poisoned and even assassinated. And all have experienced a profound grief and frustration when friends and families who would not heed their warnings fell sick and died.

Their cumulative sacrifice is their gift to you—freely given—so that you will choose to protect yourself and those you love and encourage others to do the same. As each of us passes this priceless gift on to other men and women, we increase the chances for good health and life—person by person, family by family, and community by community.

This is their hoped-for reward—that as a result of their contributions to science and medicine, you and those you love will live—and that your children will grow up healthy and fertile and produce future generations who are the same.

What you have learned may be priceless intelligence, but it is not convenient. The fact that mRNA technology maims and kills has profound implications. Given who is applying this technology, it radically alters our understanding of whom we can trust—not just about mRNA technology but about a far wider range of issues that touch numerous aspects of our daily life and finances.

Off the list of trusted institutions are our governments, including the military and the agencies that regulate health. Off the list is the pharmaceutical industry. Off the list are the many doctors and hospitals that were paid richly to push mRNA vaccines, and even before that to administer harmful and often lethal COVID-19 treatments. Off the list are the media that made war on the hearts and minds of people everywhere, filling them with fear to herd them and their children into the mRNA "kill box."

There were also many courageous people who were not surprised to learn that mRNA technology maims and kills. These included the author of the foreword to this book, Mary Holland. Mary is the co-editor of *Turtles All the Way Down*, a formidable review of the cascade of lies used to prop up the vaccine industry (originally published in Hebrew in 2019). Mary and Robert F. Kennedy, Jr. and their colleagues at Children's Health Defense have worked for years to protect children

from an onslaught of dangerous pharmaceuticals, the debasement of our food system, increases in EMF radiation, and other forms of environmental poisons and toxicity. Another courageous figure is Dr. David Rasnick, who authored the chapter in this book regarding the HIV/AIDS lies used to engineer and fund many aspects of the regulatory infrastructure that created, financed, and delivered mRNA vaccines.

I, too, was among the group not surprised by the mRNA technology's intentionally destructive effects. After trillions of dollars started to go missing from the U.S. government, I began in 2000 to warn Americans that our retirements and social safety nets depended on simple mathematical formulas. If we continued to permit trillions to be stolen, then the financial books would be balanced by other methods. These would include curtailing or inflating away financial and health benefits, implementing delayed retirement ages, intentionally lowering life expectancy, or some combination thereof. Indeed, for the last two decades, a wide number of policies—a Great Poisoning—has caused a steady drop in life expectancy. Currently, at least 54% of American children have one or more chronic diseases. When I served as an investment advisor from 2007 to 2018, I had clients whose children suffered from vaccine injury, and I saw first-hand the devastating personal and financial consequences of such injuries.

Finally, also among the group of clear-eyed scientists was economist Dr. Mark Skidmore. Since 2017, Dr. Skidmore has helped to document the trillions missing from the U.S. government. In addition, his survey of the impact of COVID-19 and the COVID-19 vaccines, published in 2022 and 2023, has helped to document the extraordinary levels of sickness, disability, and death resulting from COVID-19 vaccines and related mandates and coercive measures.

As you face the challenges ahead to protect yourself and your family from mRNA technology, you will also face many questions about how to protect yourself and your loved ones from an establishment that not only has failed us but is engineering a coup d'état—including a fundamental change in our human rights and property rights.

My pastor in Washington always used to say, "If we can face it, God can fix it." In closing *mRNA Vaccine Toxicity*, we pray that you will face the risks of mRNA technology and its wider implications and that you will use that knowledge to protect as many people as you possibly can. If you currently work in or finance this killing machinery, we pray that

you will shift your time and support out of that which brings death and poverty toward that which gives life and builds wealth.

Choose life and help those you love do the same. Our future depends on it.

# References


[1] Moderna Inc.: *Moderna 2023 proxy statement*. 2023. URL: https://archive.org/details/moderna-proxy-statement-2023.

[2] T. Binder: *The Prevailing Corona Nonsense Narrative, Debunked in 10 or 26 Minutes*. 2021. URL: https://doctors4covidethics.org/the-prevailing-corona-nonsense-narrative-debunked-in-10-or-26-minutes/.

[3] L. Yan et al.: Unusual Features of the SARS-CoV-2 Genome Suggesting Sophisticated Laboratory Modification Rather Than Natural Evolution and Delineation of Its Probable Synthetic Route. *Preprint* (2020). DOI: 10.5281/zenodo.4028830.

[4] L. Yan et al.: SARS-CoV-2 Is an Unrestricted Bioweapon: A Truth Revealed through Uncovering a Large-Scale, Organized Scientific Fraud. *Preprint* (2020). DOI: 10.5281/zenodo.4073131.

[5] K. Schwab and T. Malleret: *COVID-19: The Great Reset*. Forum Publishing, 2020.

[6] D. G. Rancourt et al.: *Evaluation of the virulence of SARS-CoV-2 in France, from all-cause mortality 1946-2020*. 2020. URL: https://denisrancourt.ca/entries.php?id=10.

[7] R. B. Brown: Public health lessons learned from biases in coronavirus mortality overestimation. *Disaster Med. Public Health Prep.* (2020), 1–24. PMID: 32782048.

[8] J. P. A. Ioannidis: Infection fatality rate of COVID-19 inferred from seroprevalence data. *Bull. World Health Organ.* (2020), BLT.20.265892. URL: https://www.who.int/bulletin/online_first/BLT.20.265892.pdf.

[9] J. P. A. Ioannidis: Reconciling estimates of global spread and infection fatality rates of COVID-19: An overview of systematic evaluations. *Eur. J. Clin. Invest.* 5 (2021), e133554. PMID: 33768536.

[10] P. A. McCullough et al.: Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19). *Reviews in cardiovascular medicine* 21 (2020), 517–530. PMID: 33387997.

[11] P. E. Marik et al.: A scoping review of the pathophysiology of COVID-19. *Int. J. Immunopathol. Pharmacol.* 35 (2021), 20587384211048026. PMID: 34569339.

[12] Anonymous: *WHO advises that ivermectin only be used to treat COVID-19 within clinical trials*. 2021. URL: https://www.who.int/news-room/feature-stories/detail/who-advises-that-ivermectin-only-be-used-to-treat-covid-19-within-clinical-trials.

[13] N. Hanna et al.: Detection of Messenger RNA COVID-19 Vaccines in Human Breast Milk. *JAMA pediatrics* (2022). PMID: 36156636.

[14] U.S. National Library of Medicine: *ClinicalTrials.gov*. 2022. URL: ClinicalTrials.gov.

[15] D. M. Knipe and P. M. Howley: *Fields Virology*. Wolters Kluwer, 2013.

[16] P. J. Delves et al.: *Roitt's Essential Immunology*. Wiley Blackwell, 2017.

[17] P. Marik: *An overview of the MATH+, I-MASK+ and I-RECOVER Protocols (A Guide to the Management of COVID-19)*. 2021. URL: https://covid19criticalcare.com/wp-content/uploads/2020/12/FLCCC-Protocols-%E2%80%93-A-Guide-to-the-Management-of-COVID-19.pdf.

[18] S. Bhakdi and J. Tranum-Jensen: Molecular nature of the complement lesion. *Proc. Natl. Acad. Sci. U. S. A.* 75 (1978), 5655–5659. PMID: 281714.

[19] J. Tranum-Jensen et al.: Complement lysis: the ultrastructure and orientation of the C5b-9 complex on target sheep erythrocyte membranes. *Scandinavian journal of immunology* 7 (1978), 45–6. PMID: 635472.

[20] K. Karikó et al.: Suppression of RNA recognition by Toll-like receptors: the impact of nucleoside modification and the evolutionary origin of RNA. *Immunity* 23 (2005), 165–75. PMID: 16111635.

[21] T. G. Kimman et al.: Local and systemic antibody response to bovine respiratory syncytial virus infection and reinfection in calves with and without maternal antibodies. *Journal of clinical microbiology* 25 (1987), 1097–106. PMID: 2954996.

[22] S. Crotty et al.: Cutting edge: long-term B cell memory in humans after smallpox vaccination. *J. Immunol.* 171 (2003), 4969–73. PMID: 14607890.

[23] L. Yang et al.: Waning immunity and re-emergence of measles and mumps in the vaccine era. *Curr. Opin. Virol.* 40 (2020), 48–54. PMID: 32634672.

[24] S. Vygen et al.: Waning immunity against mumps in vaccinated young adults, France 2013. *Euro Surveill.* 21 (2016), 30156. PMID: 26987576.

[25] J. Qu et al.: Profile of Immunoglobulin G and IgM Antibodies Against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Clin. Infect. Dis.* 71 (2020), 2255–2258. PMID: 32337590.

[26] S. S. Nielsen et al.: SARS-CoV-2 elicits robust adaptive immune responses regardless of disease severity. *EBioMedicine* 68 (2021), 103410. PMID: 34098342.

[27] M. Dugas et al.: Less severe course of COVID-19 is associated with elevated levels of antibodies against seasonal human coronaviruses OC43 and HKU1 (HCoV OC43, HCoV HKU1). *Int. J. Infect. Dis.* 105 (2021), 304–306. PMID: 33636357.

[28] J. Mateus et al.: Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. *Science* 370 (2020), 89–94. PMID: 32753554.

[29] A. Grifoni et al.: Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. *Cell* 181 (2020), 1489–1501.e15. PMID: 32473127.

[30] C.-T. Tseng et al.: Immunization with SARS coronavirus vaccines leads to pulmonary immunopathology on challenge with the SARS virus. *PLoS One* 7 (2012), e35421. PMID: 22536382.

[31] C. Y. Yong et al.: Recent Advances in the Vaccine Development Against Middle East Respiratory Syndrome-Coronavirus. *Front. Microbiol.* 10 (2019), 1781. PMID: 31428074.

[32] M. Cloutier et al.: ADE and hyperinflammation in SARS-CoV2 infection—comparison with dengue hemorrhagic fever and feline infectious peritonitis. *Cytokine* 136 (2020), 155256. PMID: 32866898.

[33] W. S. Lee et al.: Antibody-dependent enhancement and SARS-CoV-2 vaccines and therapies. *Nat. Microbiol.* 5 (2020), 1185–1191. PMID: 32908214.

[34] J. A. Tetro: Is COVID-19 receiving ADE from other coronaviruses? *Microbes and infection* 22 (2020), 72–73. PMID: 32092539.

[35] H. Ulrich et al.: Dengue Fever, COVID-19 (SARS-CoV-2), and Antibody-Dependent Enhancement (ADE): A Perspective. *Cytometry A* 97 (2020), 662–667. PMID: 32506725.

[36] A. B. Schuren et al.: Recent advances in viral evasion of the MHC Class I processing pathway. *Curr. Opin. Immunol.* 40 (2016), 43–50. PMID: 27065088.

[37] Y. Kurono: The mucosal immune system of the upper respiratory tract and recent progress in mucosal vaccines. *Auris nasus larynx* (2021). DOI: 10.1016/j.anl.2021.07.003.

[38] J. R. McGhee et al.: The mucosal immune system: from fundamental concepts to vaccine development. *Vaccine* 10 (1992), 75–88. PMID: 1539467.

[39] M. H. Kim et al.: Superior immune responses induced by intranasal immunization with recombinant adenovirus-based vaccine expressing full-length Spike protein of Middle East respiratory syndrome coronavirus. *PLoS One* 14 (2019), e0220196. PMID: 31329652.

[40] L. Meyer-Arndt et al.: Cutting Edge: Serum but Not Mucosal Antibody Responses Are Associated with Pre-Existing SARS-CoV-2 Spike Cross-Reactive CD4+ T Cells following BNT162b2 Vaccination in the Elderly. *J. Immunol.* 208 (2022), 1001–1005. PMID: 35121642.

[41] E. Martinuzzi et al.: A Single Dose of BNT162b2 mRNA Vaccine Induces Airway Immunity in SARS-CoV-2 Naive and recovered COVID-19 subjects. *Clin. Infect. Dis.* (2022). PMID: 35579991.

[42] N. V. V. Chau et al.: *Transmission of SARS-CoV-2 Delta Variant Among Vaccinated Healthcare Workers, Vietnam*. 2021. DOI: 10.2139/ssrn.3897733.

[43] A. Singanayagam et al.: Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *Lancet Infect. Dis.* (2021). DOI: 10.1016/s1473-3099(21)00648-4.

[44] H. Wang et al.: Development of an Inactivated Vaccine Candidate, BBIBP-CorV, with Potent Protection against SARS-CoV-2. *Cell* 182 (2020), 713–721.e9. PMID: 32778225.

[45] E. Twentyman et al.: Interim Recommendation of the Advisory Committee on Immunization Practices for Use of the Novavax COVID-19 Vaccine in Persons Aged ≥18 years—United States, July 2022. *MMWR* 71 (2022), 988–992. DOI: 10.15585/mmwr.mm7131a2.

[46] D.-H. Kang et al.: Fulminant Giant Cell Myocarditis following Heterologous Vaccination of ChAdOx1 nCoV-19 and Pfizer-BioNTech COVID-19. *Medicina* 58 (2022). PMID: 35334625.

[47] S. Kazama et al.: Biopsy-Proven Fulminant Myocarditis Requiring Mechanical Circulatory Support Following COVID-19 mRNA Vaccination. *CJC Open* 4 (2022), 501–505. PMID: 35187464.

[48] H. Jafari et al.: Polio eradication. Efficacy of inactivated poliovirus vaccine in India. *Science* 345 (2014), 922–5. PMID: 25146288.

[49] P. Guermonprez and S. Amigorena: Pathways for antigen cross presentation. *Springer Semin. Immunopathol.* 26 (2005), 257–71. PMID: 15592842.

[50] D. Sengupta et al.: Proteasomal degradation within endocytic organelles mediates antigen cross-presentation. *EMBO J.* 38 (2019), e99266. PMID: 31271236.

[51] L. Qin et al.: Evolution of and evolutionary relationships between extant vaccinia virus strains. *J. Virol.* 89 (2015), 1809–24. PMID: 25410873.

[52] M. J. Babic: Eczema vaccinatum: a reaction to the smallpox vaccine. A report of a rare but potentially lethal consequence. *Am. J. Nurs.* 107 (2007), 30–1. PMID: 17667384.

[53] S. L. Nuismer et al.: Eradicating infectious disease using weakly transmissible vaccines. *Proc. Biol. Sci.* 283 (2016). PMID: 27798311.

[54] A. J. Basinski et al.: Evaluating the promise of recombinant transmissible vaccines. *Vaccine* 36 (2018), 675–682. PMID: 29279283.

[55] C. C. Burns et al.: Multiple Independent Emergences of Type 2 Vaccine-Derived Polioviruses during a Large Outbreak in Northern Nigeria. *J. Virol.* 87 (2013), 4907–4922. PMID: 23408630.

[56] O. Andries et al.: N[1]-methylpseudouridine-incorporated mRNA outperforms pseudouridine-incorporated mRNA by providing enhanced protein expression and reduced immunogenicity in mammalian cell lines and mice. *J. Control. Release* 217 (2015), 337–344. PMID: 26342664.

[57] N. Pardi et al.: Nucleoside-modified mRNA vaccines induce potent T follicular helper and germinal center B cell responses. *J. Exp. Med.* 215 (2018), 1571–1588. PMID: 29739835.

[58] Anonymous: *EMA Assessment report: COVID-19 Vaccine Moderna*. 2021. URL: https://www.ema.europa.eu/en/documents/assessment-report/spikevax-previously-covid-19-vaccine-moderna-epar-public-assessment-report_en.pdf.

[59] Anonymous: *FDA briefing document: Pfizer-BioNTech COVID-19 Vaccine*. 2020. URL: https://www.fda.gov/media/144245/download.

[60] Anonymous: *EMA Assessment report: Comirnaty*. 2021. URL: https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf.

[61] P. D. Thacker: Covid-19: Researcher blows the whistle on data integrity issues in Pfizer's vaccine trial. *BMJ* (2021), n2635. DOI: 10.1136/bmj.n2635.

[62] M. Palmer et al.: *On the use of the Pfizer and the Moderna COVID-19 mRNA vaccines in children and adolescents*. 2022. URL: https://doctors4covidethics.org/on-the-use-of-the-pfizer-and-the-moderna-covid-19-mrna-vaccines-in-children-and-adolescents/.

[63] A. F. Ogata et al.: Circulating SARS-CoV-2 Vaccine Antigen Detected in the Plasma of mRNA-1273 Vaccine Recipients. *Clin. Infect. Dis.* 74 (2022), 715–718. PMID: 34015087.

[64] S. Bansal et al.: Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer-BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mRNA Vaccines. *J. Immunol.* 207 (2021), 2405–2410. PMID: 34654691.

[65] M. Palmer and S. Bhakdi: *Long-term persistence of the SARS-CoV-2 spike protein: evidence and implications*. 2021. URL: https://doctors4covidethics.org/long-term-persistence-of-the-sars-cov-2-spike-protein-evidence-and-implications-2/.

[66] K. Röltgen et al.: Immune imprinting, breadth of variant recognition and germinal center response in human SARS-CoV-2 infection and vaccination. *Cell* (2022). PMID: 35148837.

[67] E. Magen et al.: Clinical and Molecular Characterization of a Rare Case of BNT162b2 mRNA COVID-19 Vaccine-Associated Myositis. *Vaccines* 10 (2022). PMID: 35891299.

[68] M. A. Bruusgaard-Mouritsen et al.: Clinical manifestations and impact on daily life of allergy to polyethylene glycol (PEG) in ten patients. *Clin. Exp. Allerg.* (2021). PMID: 33394522.

[69] L. Klimek et al.: Allergenic components of the mRNA-1273 vaccine for COVID-19: possible involvement of polyethylene glycol and IgG-mediated complement activation. *Allergy* (2021). PMID: 33657648.

[70] A. Troelnikov et al.: Basophil reactivity to BNT162b2 is mediated by PEGylated lipid nanoparticles in PEG allergic patients. *J. Allerg. Clin. Immunol.* (2021). PMID: 33991580.

[71] M. Li et al.: Myocarditis or Pericarditis Following the COVID-19 Vaccination in Adolescents: A Systematic Review. *Vaccines* 10 (2022). PMID: 36016204.

[72] B. Shilhavy: *43,898 Dead, 4,190,493 Injured Following COVID Vaccines in European Database of Adverse Reactions.* 2022. URL: https://healthimpactnews.com/2022/43898-dead-4190493-injured-following-covid-19-vaccines-in-european-database-of-adverse-reactions/.

[73] Y. Wang et al.: Cross-reaction of SARS-CoV antigen with autoantibodies in autoimmune diseases. *Cell. Mol. Immunol.* 1 (2004), 304–7. PMID: 16225774.

[74] M. F. Cusick et al.: Molecular mimicry as a mechanism of autoimmune disease. *Clin. Rev. Allergy Immunol.* 42 (2012), 102–11. PMID: 22095454.

[75] K. T. Coppieters et al.: Viral infections and molecular mimicry in type 1 diabetes. *APMIS* 120 (2012), 941–9. PMID: 23051179.

[76] G. Halpert and Y. Shoenfeld: SARS-CoV-2, the autoimmune virus. *Autoimmun. Rev.* 19 (2020), 102695. PMID: 33130000.

[77] Y. Chen et al.: New-onset autoimmune phenomena post-COVID-19 vaccination. *Immunology* 165 (2022), 386–401. PMID: 34957554.

[78] J. Lyons-Weiler: Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity. *Journal of translational autoimmunity* 3 (2020), 100051. PMID: 32292901.

[79] D. Kanduc and Y. Shoenfeld: Molecular mimicry between SARS-CoV-2 spike glycoprotein and mammalian proteomes: implications for the vaccine. *Immunol. Res.* 68 (2020), 310–313. PMID: 32946016.

[80] L. E. Muñoz et al.: Autoimmunity and chronic inflammation—two clearance-related steps in the etiopathogenesis of SLE. *Autoimmun. Rev.* 10 (2010), 38–42. PMID: 20817127.

[81] C. A. Cañas et al.: Patients with relapsing polychondritis and previous cartilage trauma present more autoimmunity phenomena. *Rheumatol. Int.* 32 (2012), 541–3. PMID: 21267573.

[82] F. Tanriverdi et al.: Investigation of antihypothalamus and antipituitary antibodies in amateur boxers: is chronic repetitive head trauma-induced pituitary dysfunction associated with autoimmunity? *Eur. J. Endocrinol.* 162 (2010), 861–7. PMID: 20176736.

[83] R. W. Frenck et al.: Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. *N. Engl. J. Med.* (2021). PMID: 34043894.

[84] K. Ali et al.: Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents. *N. Engl. J. Med.* (2021). PMID: 34379915.

[85] S. Ndeupen et al.: The mRNA-LNP platform's lipid nanoparticle component used in preclinical vaccine studies is highly inflammatory. *iScience* 24 (2021), 103479. PMID: 34841223.

[86] F. Bril et al.: Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: Causality or casualty? *J. Hepatol.* 75 (2021), 222–224. PMID: 33862041.

[87] P. Caron: Autoimmune and inflammatory thyroid diseases following vaccination with SARS-CoV-2 vaccines: from etiopathogenesis to clinical management. *Endocrine* (2022). PMID: 35763241.

[88] M. E. Mingot-Castellano et al.: COVID-19 Vaccines and Autoimmune Hematologic Disorders. *Vaccines* 10 (2022). PMID: 35746569.

[89] A. Pujol et al.: Thyroid as a target of adjuvant autoimmunity/inflammatory syndrome due to mRNA-based SARS-CoV2 vaccination: from Graves' disease to silent thyroiditis. *J. Endocrinol. Invest.* 45 (2022), 875–882. PMID: 34792795.

[90] A. Català et al.: Cutaneous reactions after SARS-COV-2 vaccination: A cross-sectional Spanish nationwide study of 405 cases. *Br. J. Dermatol.* (2021). PMID: 34254291.

[91] K. Ajmera et al.: Gastrointestinal Complications of COVID-19 Vaccines. *Cureus* 14 (2022), e24070. PMID: 35573556.

[92] Y.-T. Hung et al.: Haemorrhagic bullous pyoderma gangrenosum following COVID-19 vaccination. *J. Eur. Acad. Dermatol. Venereol.* (2022). PMID: 35398933.

[93] J. Mitchell and Q.-Y. Yue: Appendicitis as a possible safety signal for the COVID-19 vaccines. *Vaccine X* 9 (2021), 100122. PMID: 34746743.

[94] U. Krüger: *COVID vaccination and turbo cancer: pathological evidence*. 2022. URL: https://doctors4covidethics.org/covid-vaccination-and-turbo-cancer-pathological-evidence/.

[95] Z. Qin et al.: Pre-exposure to mRNA-LNP inhibits adaptive immune responses and alters innate immune fitness in an inheritable fashion. *PLoS Pathog.* 18 (2022), e1010830. PMID: 36054264.

[96] A. V. Letarov et al.: Free SARS-CoV-2 Spike Protein S1 Particles May Play a Role in the Pathogenesis of COVID-19 Infection. *Biochemistry Mosc* 86 (2021), 257–261. PMID: 33838638.

[97] S. Belham: *Histology World*. 2022. URL: http://www.histology-world.com/.

[98] T. Iino et al.: Polyarteritis nodosa with aortic dissection: necrotizing vasculitis of the vasa vasorum. *J. Rheumatol.* 19 (1992), 1632–6. PMID: 1361205.

[99] B. M. Voorzaat et al.: Alpha-1 Antitrypsin Deficiency Presenting with MPO-ANCA Associated Vasculitis and Aortic Dissection. *Case Rep. Med.* 2017 (2017), 8140641. PMID: 28367219.

[100] A. Ramandi et al.: Aortic dissection and Covid-19; a comprehensive systematic review. *Current problems in cardiology* (2022), 101129. PMID: 35139402.

[101] M. A. Tuncer et al.: Causality Association Between COVID-19 Infection and Aortic Dissection. *Anatol. J. Cardiol.* 26 (2022), 338–339. PMID: 35435848.

[102] M. Takahashi et al.: An autopsy case report of aortic dissection complicated with histiolymphocytic pericarditis and aortic inflammation after mRNA COVID-19 vaccination. *Leg. Med. Tokyo* 59 (2022), 102154. PMID: 36191411.

[103] K. Chida et al.: Rupture of Vertebral Artery Dissecting Aneurysm after mRNA Anti-COVID-19 Vaccination: A Report of Two Cases. *NMC Case Rep. J.* 9 (2022), 95–100. PMID: 35646499.

[104] K. M. Chue et al.: Spontaneous rare visceral pseudoaneurysm presenting with rupture after COVID-19 vaccination. *ANZ J. Surg.* 92 (2022), 915–917. PMID: 34480824.

[105] B. H. Kim and M. C. Yoo: Intracranial Hemorrhage Due to Potential Rupture of an Arteriovenous Malformation after BNT162b2 COVID-19 mRNA Vaccination in a Young Korean Woman: Case Report. *Vaccines* 10 (2022). PMID: 35334996.

[106] S. Oshida et al.: Intracranial aneurysm rupture within three days after receiving mRNA anti-COVID-19 vaccination: Three case reports. *Surg. Neurol. Int.* 13 (2022), 117. PMID: 35509565.

[107] R. Takeyama et al.: Intracerebral hemorrhage due to vasculitis following COVID-19 vaccination: a case report. *Acta Neurochir. Wien* 164 (2022), 543–547. PMID: 34783899.

[108] L. Roncati et al.: A Three-Case Series of Thrombotic Deaths in Patients over 50 with Comorbidities Temporally after modRNA COVID-19 Vaccination. *Pathogens* 11 (2022). PMID: 35456110.

[109] Y. N. Aye et al.: Acute Myocardial Infarction and Myocarditis following COVID-19 Vaccination. *QJM* (2021). PMID: 34586408.

[110] J. G. Sung et al.: Acute Myocardial Infarction Within 24 Hours After COVID-19 Vaccination. *Am. J. Cardiol.* 156 (2021), 129–131. PMID: 34364657.

[111] Y. Kawamura et al.: A case of ST segment elevation myocardial infarction within 24 h of a third dose of COVID-19 mRNA vaccine. *Cardiovasc. Revasc. Med.* (2022). PMID: 35718694.

[112] Anonymous: *OpenVAERS COVID Vaccine Data*. 2021. URL: https://www.openvaers.com/covid-data.

[113] Z. Kolahchi et al.: Acute ischemic stroke and vaccine-induced immune thrombotic thrombocytopenia post COVID-19 vaccination; a systematic review. *J. Neurol. Sci.* 439 (2022), 120327. PMID: 35752132.

[114] A. Alhashim et al.: Extensive Cerebral Venous Sinus Thrombosis (CVST) After the First Dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 Vaccine without Thrombotic Thrombocytopenia Syndrome (TTS) in a Healthy Woman. *Am. J. Case Rep.* 23 (2022), e934744. PMID: 35136010.

[115] J. Finsterer and S. Nics: Venous sinus thrombosis after the second jab of an mRNA-based SARS-CoV-2 vaccine. *Brain Hemorrhages* 3 (2022), 36–38. PMID: 34901793.

[116] M. I. A. Qureshi et al.: Venous sinus thrombosis after the first dose of Pfizer BioNTech vaccine. *BMJ Case Rep.* 15 (2022). PMID: 35606039.

[117] L. Dias et al.: Cerebral Venous Thrombosis after BNT162b2 mRNA SARS-CoV-2 vaccine. *J. Stroke Cerebrovasc. Dis.* 30 (2021), 105906. PMID: 34111775.

[118] E. Y. Ahn et al.: Pulmonary embolism and inferior vena cava thrombosis in a young male patient after mRNA-1273 (Moderna) immunization: A case report. *Tuberc. Respir. Dis. Seoul* (2022). PMID: 35822319.

[119] R. Scendoni et al.: Multiple sites of thrombosis without thrombocytopenia after a second dose of Pfizer-BioNTech COVID-19 vaccine. *Int. J. Immunopathol. Pharmacol.* 36 (2022), 3946320221128534. PMID: 36123789.

[120] T.-G. Lee et al.: Acute gastric and non-mesenteric colonic infarction following mRNA COVID-19 vaccination. *Asian J. Surg.* 45 (2022), 1469–1470. PMID: 35618584.

[121] H. Suzuki et al.: The pathophysiology of IgA nephropathy. *J. Am. Soc. Nephrol.* 22 (2011), 1795–803. PMID: 21949093.

[122] S. Nakatani et al.: New-onset kidney biopsy-proven IgA vasculitis after receiving mRNA-1273 COVID-19 vaccine: case report. *CEN Case Rep.* (2022). PMID: 35075622.

[123] K. Sugita et al.: Development of IgA vasculitis with severe glomerulonephritis after COVID-19 vaccination: a case report and literature review. *CEN Case Rep.* (2022). PMID: 35275366.

[124] B. J. DeOre et al.: SARS-CoV-2 Spike Protein Disrupts Blood-Brain Barrier Integrity via RhoA Activation. *J. Neuroimmune Pharmacol.* 16 (2021), 722–728. PMID: 34687399.

[125] S. Raghavan et al.: SARS-CoV-2 Spike Protein Induces Degradation of Junctional Proteins That Maintain Endothelial Barrier Integrity. *Frontiers Cardiovasc. Med.* 8 (2021). PMID: 34179146.

[126] H. Jiang and Y.-F. Mei: SARS-CoV-2 Spike Impairs DNA Damage Repair and Inhibits V(D)J Recombination In Vitro. *Viruses* 13 (2021), 2056. PMID: 34696485.

[127] R. N. Kostoff et al.: Why are we vaccinating children against COVID-19? *Toxicol. Rep.* 8 (2021), 1665–1684. PMID: 34540594.

[128] J. Rose and P. A. McCullough: A Report on Myocarditis Adverse Events in the U.S. Vaccine Adverse Events Reporting System (VAERS) in Association with COVID-19 Injectable Biological Products. *Current problems in cardiology* (2021), 101011. URL: https://tinyurl.com/Rose-McCullough-Myocarditis.

[129] H. Walach et al.: Experimental Assessment of Carbon Dioxide Content in Inhaled Air With or Without Face Masks in Healthy Children: A Randomized Clinical Trial. *JAMA pediatrics* (2021). PMID: 34190984.

[130] M. Skidmore: The role of social circle COVID-19 illness and vaccination experiences in COVID-19 vaccination decisions: an online survey of the United States population. *BMC Infect. Dis.* 23 (2023), 51. PMID: 36694131.

[131] A. F. Ogata et al.: Ultra-Sensitive Serial Profiling of SARS-CoV-2 Antigens and Antibodies in Plasma to Understand Disease Progression in COVID-19 Patients with Severe Disease. *Clin. Chem.* 66 (2020), 1562–1572. PMID: 32897389.

[132] H. Koiwaya et al.: Serial histopathologic assessment of fulminant myocarditis after the first mRNA COVID-19 vaccine dose. *Eur. Heart J.* 43 (2022), 1995. PMID: 35178573.

[133] C. Baumeier et al.: Intramyocardial Inflammation after COVID-19 Vaccination: An Endomyocardial Biopsy-Proven Case Series. *Int. J. Mol. Sci.* 23 (2022), 6940. PMID: 35805941.

[134] R. Ameratunga et al.: First Identified Case of Fatal Fulminant Necrotizing Eosinophilic Myocarditis Following the Initial Dose of the Pfizer-BioNTech mRNA COVID-19 Vaccine (BNT162b2, Comirnaty): an Extremely Rare Idiosyncratic Hypersensitivity Reaction. *J. Clin. Immunol.* (2022). PMID: 34978002.

[135] A. K. Verma et al.: Myocarditis after Covid-19 mRNA Vaccination. *N. Engl. J. Med.* 385 (2021), 1332–1334. PMID: 34407340.

[136] S. Choi et al.: Myocarditis-induced Sudden Death after BNT162b2 mRNA COVID-19 Vaccination in Korea: Case Report Focusing on Histopathological Findings. *J. Korean Med. Sci.* 36 (2021), e286. PMID: 34664804.

[137] J. R. Gill et al.: Autopsy Histopathologic Cardiac Findings in Two Adolescents Following the Second COVID-19 Vaccine Dose. *Arch. Pathol. Lab. Med.* (2022). PMID: 35157759.

[138] M. Mörz: A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against Covid-19. *Vaccines* 10 (2022), 2022060308. DOI: 10.3390/vaccines10101651.

[139] C. So et al.: COVID-19 mRNA vaccine-related interstitial lung disease: Two case reports and literature review. *Respirol. Case Rep.* 10 (2022), e0938. PMID: 35355663.

[140] T. Shimizu et al.: Interstitial pneumonitis after COVID-19 vaccination: A report of three cases. *Allergol. Int.* 71 (2022), 251–253. PMID: 34772608.

[141] N. M. Hughes et al.: Radiation Recall Pneumonitis on FDG PET/CT Triggered by COVID-19 Vaccination. *Clin. Nucl. Med.* 47 (2022), e281–e283. PMID: 34739397.

[142] K. Shinada et al.: Radiation recall pneumonitis after COVID-19 vaccination. *Thorac. Cancer* 13 (2022), 144–145. PMID: 34791816.

[143] C. R. Steber et al.: Rapid Development of Clinically Symptomatic Radiation Recall Pneumonitis Immediately Following COVID-19 Vaccination. *Cureus* 13 (2021), e14303. PMID: 33968515.

[144] K. McGovern et al.: Radiation recall pneumonitis in the setting of immunotherapy and radiation: a focused review. *Future Sci. OA* 5 (2019), FSO378. PMID: 31245041.

[145] S. Jarius et al.: MOG encephalomyelitis after vaccination against severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2): case report and comprehensive review of the literature. *J. Neurol.* (2022). PMID: 35737110.

[146] G. M. Asioli et al.: Anti-LGI1 encephalitis following COVID-19 vaccination: a case series. *J. Neurol.* (2022). PMID: 35751687.

[147] K. Poli et al.: Multiple Autoimmune Syndromes Including Acute Disseminated Encephalomyelitis, Myasthenia Gravis, and Thyroiditis Following Messenger Ribonucleic Acid-Based COVID-19 Vaccination: A Case Report. *Front. Neurol.* 13 (2022), 913515. PMID: 35711270.

[148] A. Vogrig et al.: Acute disseminated encephalomyelitis after SARS-CoV-2 vaccination. *Clin. Neurol. Neurosurg.* 208 (2021), 106839. PMID: 34325334.

[149] J. Werner et al.: New-onset refractory status epilepticus due to autoimmune encephalitis after vaccination against SARS-CoV-2: First case report. *Front. Neurol.* 13 (2022), 946644. PMID: 36051224.

[150] J.-J. Gao et al.: Acute encephalitis after COVID-19 vaccination: A case report and literature review. *Hum. Vaccin. Immunother.* (2022), 2082206. PMID: 35700455.

[151] K. H. Meyer zum Büschenfelde et al.: Hepatitis C virus (HCV) and autoimmune liver diseases. *Arch. Virol. Suppl.* 4 (1992), 201–4. PMID: 1333322.

[152] F. B. Bianchi: Autoimmune hepatitis: the lesson of the discovery of hepatitis C virus. *J. Hepatol.* 18 (1993), 273–5. PMID: 8228118.

[153] A. Jurado et al.: Autoimmune hepatitis type 2 and hepatitis C virus infection: study of HLA antigens. *J. Hepatol.* 26 (1997), 983–91. PMID: 9186828.

[154] Anonymous: *FDA briefing document: Moderna MRNA-1273.* 2020. URL: https://www.fda.gov/media/144452/download.

[155] L. Martin-Navarro et al.: In situ detection of vaccine mRNA in the cytoplasm of hepatocytes during COVID19 vaccine-related hepatitis. *J. Hepatol.* (2022). PMID: 36116717.

[156] T. Boettler et al.: SARS-CoV-2 vaccination can elicit a CD8 T-cell dominant hepatitis. *J. Hepatol.* 77 (2022), 653–659. PMID: 35461912.

[157] E. Vuille-Lessard et al.: Autoimmune hepatitis triggered by SARS-CoV-2 vaccination. *J. Autoimmun.* 123 (2021), 102710. PMID: 34332438.

[158] H. Shroff et al.: Liver injury following SARS-CoV-2 vaccination: A multicenter case series. *J. Hepatol.* 76 (2022), 211–214. PMID: 34339763.

[159] J. M. Pinazo-Bandera et al.: Acute hepatitis with autoimmune features after COVID-19 vaccine: coincidence or vaccine-induced phenomenon? *Gastroenterol. Rep. Oxf* 10 (2022), goac014. PMID: 35498817.

[160] A. Izagirre et al.: Autoimmune hepatitis following COVID-19 vaccination. *J. Autoimmun.* 132 (2022), 102874. PMID: 35985054.

[161] L. Camacho-Domínguez et al.: COVID-19 vaccine and autoimmunity. A new case of autoimmune hepatitis and review of the literature. *Journal of translational autoimmunity* 5 (2022), 100140. PMID: 35013724.

[162] F. Fimiano et al.: Autoimmune hepatitis or drug-induced autoimmune hepatitis following Covid-19 vaccination? *Liver Int.* 42 (2022), 1204–1205. PMID: 35230737.

[163] C. Efe et al.: Liver injury after SARS-CoV-2 vaccination: Features of immune-mediated hepatitis, role of corticosteroid therapy and outcome. *Hepatology* (2022). PMID: 35567545.

[164] A. Mahalingham et al.: First report of post-transplant autoimmune hepatitis recurrence following SARS-CoV-2 mRNA vaccination. *Transpl. Immunol.* 72 (2022), 101600. PMID: 35390478.

[165] G. S. Zin Tun et al.: Immune-mediated hepatitis with the Moderna vaccine, no longer a coincidence but confirmed. *J. Hepatol.* 76 (2022), 747–749. PMID: 34619252.

[166] F. S. Tan et al.: Acute interstitial nephritis after COVID-19 vaccination. *BMJ Case Rep.* 15 (2022). PMID: 35589264.

[167] F. S. Mira et al.: A Case of Acute Interstitial Nephritis After Two Doses of the BNT162b2 SARS-CoV-2 Vaccine. *Int. J. Nephrol. Renovasc. Dis.* 14 (2021), 421–426. PMID: 34887676.

[168] R. Fenoglio et al.: New Onset Biopsy-Proven Nephropathies after COVID Vaccination. *Am. J. Nephrol.* 53 (2022), 325–330. PMID: 35354140.

[169] T. Schaubschlager et al.: De novo or recurrent glomerulonephritis and acute tubulointerstitial nephritis after COVID-19 vaccination: A report of six cases from a single center. *Clin. Nephrol.* 97 (2022), 289–297. PMID: 35142282.

[170] A. Anderson et al.: Post-COVID-19 vaccination occurrence of splenic infarction due to arterial thrombosis. *BMJ Case Rep.* 14 (2021). PMID: 34876440.

[171] G. Kroumpouzos et al.: Cutaneous Complications of mRNA and AZD1222 COVID-19 Vaccines: A Worldwide Review. *Microorganisms* 10 (2022). PMID: 35336199.

[172] N. Nishimura et al.: IgA Vasculitis Following COVID-19 Vaccination. *Mod. Rheumatol. Case Rep.* (2022). PMID: 35253880.

[173] D. Revilla-Nebreda et al.: New-onset acral lesions on hands after administration of mRNA-1273 vaccine against SARS-CoV-2: clinical images and histopathological study of three cases. *J. Eur. Acad. Dermatol. Venereol.* 35 (2021), e747–e749. PMID: 34310777.

[174] T. Grieco et al.: COVID-19 infection and BNT162b2 vaccine triggering sarcoid-like lesions in the same patient. Response to: Sarcoid-like reaction in a patient recovering from COVID-19 pneumonia. *JAAD case reports* 23 (2022), 162–163. PMID: 35079616.

[175] S. Chopra et al.: Cutaneous skin manifestation following messenger RNA Moderna SARS-CoV-2 vaccine with dermal hypersensitivity reaction histopathology. *JAAD case reports* 16 (2021), 24–25. PMID: 34414254.

[176] V. Larson et al.: Clinical and histopathological spectrum of delayed adverse cutaneous reactions following COVID-19 vaccination. *J. Cutan. Pathol.* 49 (2021), 34–41. PMID: 34292611.

[177] M. N. Alrashdi et al.: Systemic lupus erythematosus with acute pancreatitis and vasculitic rash following COVID-19 vaccine: a case report

and literature review. *Clin. Rheumatol.* 41 (2022), 1577–1582. PMID: 35175446.

[178] A. Kreuter et al.: Induction and exacerbation of subacute cutaneous lupus erythematosus following mRNA-based or adenoviral vector-based SARS-CoV-2 vaccination. *Clin. Exp. Dermatol.* 47 (2022), 161–163. PMID: 34291477.

[179] I. Sagy et al.: New-onset systemic lupus erythematosus following BNT162b2 mRNA COVID-19 vaccine: a case series and literature review. *Rheumatol. Int.* 42 (2022), 2261–2266. PMID: 36098769.

[180] Y. J. Chee et al.: SARS-CoV-2 mRNA Vaccination and Graves' Disease: A Report of 12 Cases and Review of the Literature. *J. Clin. Endocrinol. Metab.* 107 (2022), e2324–e2330. PMID: 35235663.

[181] V. Francia et al.: The Biomolecular Corona of Lipid Nanoparticles for Gene Therapy. *Bioconjug. Chem.* 31 (2020), 2046–2059. PMID: 32786370.

[182] C. H. Kao et al.: Visualization of the transport pathways of low density lipoproteins across the endothelial cells in the branched regions of rat arteries. *Atherosclerosis* 116 (1995), 27–41. PMID: 7488331.

[183] I. Snelting-Havinga et al.: Immunoelectron microscopic visualization of the transcytosis of low density lipoproteins in perfused rat arteries. *Eur. J. Cell Biol.* 48 (1989), 27–36. PMID: 2743992.

[184] E. Vasile et al.: Visualization of the binding, endocytosis, and transcytosis of low-density lipoprotein in the arterial endothelium in situ. *J. Cell Biol.* 96 (1983), 1677–89. PMID: 6853599.

[185] K. Kucharz et al.: Post-capillary venules are the key locus for transcytosis-mediated brain delivery of therapeutic nanoparticles. *Nat. Commun.* 12 (2021), 4121. PMID: 34226541.

[186] N. Hartl et al.: From adsorption to covalent bonding: Apolipoprotein E functionalization of polymeric nanoparticles for drug delivery across the blood-brain barrier. *Adv. Ther. Weinh* 4 (2021). PMID: 33542947.

[187] B. Obermeier et al.: Development, maintenance and disruption of the blood-brain barrier. *Nat. Med.* 19 (2013), 1584–96. PMID: 24309662.

[188] N. R. Saunders et al.: The rights and wrongs of blood-brain barrier permeability studies: a walk through 100 years of history. *Front. Neurosci.* 8 (2014), 404. PMID: 25565938.

[189] M. Schlich et al.: Cytosolic delivery of nucleic acids: The case of ionizable lipid nanoparticles. *Bioeng. Transl. Med.* 6 (2021), e10213. PMID: 33786376.

[190] B. M. Bruininks et al.: A molecular view on the escape of lipoplexed DNA from the endosome. *Elife* 9 (2020). PMID: 32297853.

[191] Anonymous: *SARS-CoV-2 mRNA Vaccine (BNT162, PF-07302048) 2.6.4 [Summary statement of the pharmacokinetic study] (Japanese).* 2020.

URL: https://www.pmda.go.jp/drugs/2021/P20210212001/672212000_30300AMX00231_I100_1.pdf.

[192] Anonymous: *SARS-CoV-2 mRNA Vaccine (BNT162, PF-07302048) 2.6.4 Summary statement of the pharmacokinetic study [English translation]*. 2020. URL: https://archive.org/details/pfizer-confidential-translated.

[193] Anonymous: *Nonclinical Evaluation Report BNT162b2 [mRNA] COVID-19 vaccine (COMIRNATY™)*. 2021. URL: https://www.tga.gov.au/sites/default/files/foi-2389-06.pdf.

[194] T. P. Buzhdygan et al.: The SARS-CoV-2 spike protein alters barrier function in 2D static and 3D microfluidic in-vitro models of the human blood-brain barrier. *Neurobiol. Dis.* 146 (2020), 105131. PMID: 33053430.

[195] D. Petrovszki et al.: Penetration of the SARS-CoV-2 Spike Protein across the Blood-Brain Barrier, as Revealed by a Combination of a Human Cell Culture Model System and Optical Biosensing. *Biomedicines* 10 (2022). PMID: 35052867.

[196] T. E. Fertig et al.: Vaccine mRNA Can Be Detected in Blood at 15 Days Post-Vaccination. *Biomedicines* 10 (2022), 1538. PMID: 35884842.

[197] J. A. S. Castruita et al.: SARS-CoV-2 spike RNA vaccine sequences circulate in blood up to 28 days after COVID-19 vaccination. *APMIS* 131 (2023), 128–132. PMID: 36647776.

[198] P. Rzymski and A. Fal: To aspirate or not to aspirate? Considerations for the COVID-19 vaccines. *Pharmacol. Rep.* (2022). PMID: 35320581.

[199] B. Workman: Safe injection techniques. *Nurs. Stand.* 13 (1999), 47–53; quiz 54. PMID: 10497490.

[200] M. R. Weir: Intravascular injuries from intramuscular penicillin. *Clin. Pediatr. Phila* 27 (1988), 85–90. PMID: 3276426.

[201] T. Middleton et al.: Complications of injectable testosterone undecanoate in routine clinical practice. *Eur. J. Endocrinol.* 172 (2015), 511–7. PMID: 25637074.

[202] C. Li et al.: Intravenous injection of COVID-19 mRNA vaccine can induce acute myopericarditis in mouse model. *Clin. Infect. Dis.* (2021). PMID: 34406358.

[203] C. Lubich et al.: The Mystery of Antibodies Against Polyethylene Glycol (PEG) - What do we Know? *Pharm. Res.* 33 (2016), 2239–49. PMID: 27271335.

[204] P. Sellaturay et al.: Polyethylene Glycol-Induced Systemic Allergic Reactions (Anaphylaxis). *J. Allerg. Clin. Immunol.* 9 (2021), 670–675. PMID: 33011299.

[205] G. T. Kozma et al.: Anti-PEG antibodies: Properties, formation, testing and role in adverse immune reactions to PEGylated nano-biopharmaceuticals. *Adv. Drug Deliv. Rev.* 154-155 (2020), 163–175. PMID: 32745496.

[206] T. L. Cheng et al.: Accelerated clearance of polyethylene glycol-modified proteins by anti-polyethylene glycol IgM. *Bioconjug. Chem.* 10 (1999), 520–8. PMID: 10346886.

[207] C. Lonez et al.: Cationic lipids activate intracellular signaling pathways. *Adv. Drug Deliv. Rev.* 64 (2012), 1749–58. PMID: 22634161.

[208] D. Christensen et al.: Cationic liposomes as vaccine adjuvants. *Expert review of vaccines* 10 (2011), 513–21. PMID: 21506648.

[209] M.-G. Alameh et al.: Lipid nanoparticles enhance the efficacy of mRNA and protein subunit vaccines by inducing robust T follicular helper cell and humoral responses. *Immunity* 54 (2021), 2877–2892.e7. PMID: 34852217.

[210] J. Jarczak et al.: Defensins: natural component of human innate immunity. *Hum. Immunol.* 74 (2013), 1069–1079. PMID: 23756165.

[211] F. Milletti: Cell-penetrating peptides: classes, origin, and current landscape. *Drug Discov. Today* 17 (2012), 850–60. PMID: 22465171.

[212] S. Rajagopal et al.: Eight gram-negative bacteria are 10,000 times more sensitive to cationic detergents than to anionic detergents. *Can. J. Microbiol.* 49 (2003), 775–9. PMID: 15162202.

[213] J. Yu et al.: Integrative proteomics and metabolomics analysis reveals the toxicity of cationic liposomes to human normal hepatocyte cell line L02. *Molecular omics* 14 (2018), 362–372. PMID: 30247494.

[214] C. C. Winterbourn: Reconciling the chemistry and biology of reactive oxygen species. *Nat. Chem. Biol.* 4 (2008), 278–86. PMID: 18421291.

[215] W. L. Nyhan: Disorders of purine and pyrimidine metabolism. *Mol. Genet. Metab.* 86 (2005), 25–33. PMID: 16176880.

[216] M. C. Filion and N. C. Phillips: Toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells. *Biochim. Biophys. Acta* 1329 (1997), 345–56. PMID: 9371426.

[217] G. A. Hazelton and C. A. Lang: Glutathione contents of tissues in the aging mouse. *Biochem. J.* 188 (1980), 25–30. PMID: 7406884.

[218] I. Urits et al.: A Review of Patisiran (ONPATTRO®) for the Treatment of Polyneuropathy in People with Hereditary Transthyretin Amyloidosis. *Neurol. Ther.* 9 (2020), 301–315. PMID: 32785879.

[219] D. Adams et al.: Long-term safety and efficacy of patisiran for hereditary transthyretin-mediated amyloidosis with polyneuropathy: 12-month results of an open-label extension study. *Lancet Neurol.* 20 (2021), 49–59. PMID: 33212063.

[220] H. Lin et al.: Experience of patisiran with transthyretin stabilizers in patients with hereditary transthyretin-mediated amyloidosis. *Neurodegener. Dis. Manag.* 10 (2020), 289–300. PMID: 32519928.

[221] J. F. Apgar et al.: Quantitative Systems Pharmacology Model of hUGT1A1-modRNA Encoding for the UGT1A1 Enzyme to Treat Crigler-Najjar Syndrome Type 1. *CPT Pharmacometrics Syst. Pharmacol.* 7 (2018), 404–412. PMID: 29637732.

[222] D. Garde: *Lavishly funded Moderna hits safety problems in bold bid to revolutionize medicine.* 2017. URL: https://www.statnews.com/2017/01/10/moderna-trouble-mrna/.

[223] W. Webb: *Moderna's "Hail Mary".* 2021. URL: https://unlimitedhangout.com/modernas-hail-mary/.

[224] Anonymous: *Investigation of metallic contaminations found in vector- and mRNA-based COVID-19-"vaccines": Preliminary Results.* 2022. URL: https://doctors4covidethics.org/investigation-of-metallic-contaminations-found-in-vector-and-mrna-based-covid-19-vaccines-preliminary-results/.

[225] K. McKernan et al.: *Sequencing of bivalent Moderna and Pfizer mRNA vaccines reveals nanogram to microgram quantities of expression vector dsDNA per dose.* 2023. DOI: 0.31219/osf.io/b9t7m.

[226] M. Schmeling et al.: Batch-dependent safety of the BNT162b2 mRNA COVID-19 vaccine. *Eur. J. Clin. Invest.* (2023), e13998. PMID: 36997290.

[227] A. Stewart et al.: Malignant disease in childhood and diagnostic irradiation in utero. *Lancet* 271 (1956), 447. PMID: 13358242.

[228] A. Stewart and G. W. Kneale: Radiation dose effects in relation to obstetric x-rays and childhood cancers. *Lancet* 1 (1970), 1185–8. PMID: 4192374.

[229] E. B. Harvey et al.: Prenatal x-ray exposure and childhood cancer in twins. *N. Engl. J. Med.* 312 (1985), 541–5. PMID: 3969117.

[230] R. Wakeford: Childhood leukaemia following medical diagnostic exposure to ionizing radiation in utero or after birth. *Radiat. Prot. Dosimetry* 132 (2008), 166–74. PMID: 18922822.

[231] Y. Suzuki et al.: The micronucleus test and erythropoiesis. Effects of erythropoietin and a mutagen on the ratio of polychromatic to normochromatic erythrocytes (P/N ratio). *Mutagenesis* 4 (1989), 420–4. PMID: 2516221.

[232] J. A. Heddle et al.: The induction of micronuclei as a measure of genotoxicity. A report of the U.S. Environmental Protection Agency Gene-Tox Program. *Mutat. Res.* 123 (1983), 61–118. PMID: 6888413.

[233] S. Sommer et al.: Micronucleus Assay: The State of Art, and Future Directions. *Int. J. Mol. Sci.* 21 (2020). PMID: 32102335.

[234] C. T. Inglut et al.: Immunological and Toxicological Considerations for the Design of Liposomes. *Nanomaterials* 10 (2020). PMID: 31978968.

[235] D. Baltimore: RNA-dependent DNA polymerase in virions of RNA tumour viruses. *Nature* 226 (1970), 1209–11. PMID: 4316300.

[236] S. Spiegelman et al.: Characterization of the products of RNA-directed DNA polymerases in oncogenic RNA viruses. *Nature* 227 (1970), 563–7. PMID: 4317039.

[237] Y. Sakaki et al.: The LINE-1 family of primates may encode a reverse transcriptase-like protein. *Cold Spring Harb. Symp. Quant. Biol.* 51 Pt 1 (1986), 465–9. PMID: 2438081.

[238] P. Klenerman et al.: A non-retroviral RNA virus persists in DNA form. *Nature* 390 (1997), 298–301. PMID: 9384383.

[239] M. B. Geuking et al.: Recombination of retrotransposon and exogenous RNA virus results in nonretroviral cDNA integration. *Science* 323 (2009), 393–6. PMID: 19150848.

[240] C. Esnault et al.: Human LINE retrotransposons generate processed pseudogenes. *Nat. Genet.* 24 (2000), 363–7. PMID: 10742098.

[241] R. Cordaux and M. A. Batzer: The impact of retrotransposons on human genome evolution. *Nature reviews. Genetics* 10 (2009), 691–703. PMID: 19763152.

[242] W. Ding et al.: L1 elements, processed pseudogenes and retrogenes in mammalian genomes. *IUBMB Life* 58 (2006), 677–85. PMID: 17424906.

[243] I. Ovchinnikov et al.: Genomic characterization of recent human LINE-1 insertions: evidence supporting random insertion. *Genome Res.* 11 (2001), 2050–8. PMID: 11731495.

[244] C. R. Beck et al.: LINE-1 Elements in Structural Variation and Disease. *Annu. Rev. Genomics Hum. Genet.* 12 (2011), 187–215. PMID: 21801021.

[245] J. R. Kemp and M. S. Longworth: Crossing the LINE Toward Genomic Instability: LINE-1 Retrotransposition in Cancer. *Front. Chem.* 3 (2015), 68. PMID: 26734601.

[246] S. Kubo et al.: L1 retrotransposition in nondividing and primary human somatic cells. *Proc. Natl. Acad. Sci. U. S. A.* 103 (2006), 8036–41. PMID: 16698926.

[247] I. Georgiou et al.: Retrotransposon RNA expression and evidence for retrotransposition events in human oocytes. *Hum. Mol. Genet.* 18 (2009), 1221–8. PMID: 19147684.

[248] V. A. Belyi et al.: Unexpected inheritance: multiple integrations of ancient bornavirus and ebolavirus/marburgvirus sequences in vertebrate genomes. *PLoS Pathog.* 6 (2010), e1001030. PMID: 20686665.

[249] M. Horie et al.: Endogenous non-retroviral RNA virus elements in mammalian genomes. *Nature* 463 (2010), 84–7. PMID: 20054395.

[250] M. Horie and K. Tomonaga: Non-retroviral fossils in vertebrate genomes. *Viruses* 3 (2011), 1836–48. PMID: 22069518.

[251] A. Katzourakis and R. J. Gifford: Endogenous viral elements in animal genomes. *PLoS Genet.* 6 (2010), e1001191. PMID: 21124940.

[252] S. Chiba et al.: Widespread endogenization of genome sequences of non-retroviral RNA viruses into plant genomes. *PLoS Pathog.* 7 (2011), e1002146. PMID: 21779172.

[253] E. V. Koonin: Taming of the shrewd: novel eukaryotic genes from RNA viruses. *BMC Biol.* 8 (2010), 2. PMID: 20067611.

[254] H. Liu et al.: Widespread horizontal gene transfer from double-stranded RNA viruses to eukaryotic nuclear genomes. *J. Virol.* 84 (2010), 11876–87. PMID: 20810725.

[255] O. Dhellin et al.: Functional differences between the human LINE retrotransposon and retroviral reverse transcriptases for in vivo mRNA reverse transcription. *EMBO J.* 16 (1997), 6590–602. PMID: 9351839.

[256] L. Zhang et al.: Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues. *Proc. Natl. Acad. Sci. U. S. A.* 118 (2021). PMID: 33958444.

[257] M. Aldén et al.: Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line. *Curr. Issues Mol. Biol.* 44 (2022), 1115–1126. PMID: 35723296.

[258] D. C. Hancks and H. H. Kazazian: Active human retrotransposons: variation and disease. *Curr. Opin. Genet. Dev.* 22 (2012), 191–203. PMID: 22406018.

[259] M. Palmer and J. Gilthorpe: *COVID-19 mRNA vaccines contain excessive quantities of bacterial DNA: evidence and implications.* 2023. URL: https://doctors4covidethics.org/covid-19-mrna-vaccines-contain-excessive-quantities-of-bacterial-dna-evidence-and-implications/.

[260] P. J. Southern and P. Berg: Transformation of mammalian cells to antibiotic resistance with a bacterial gene under control of the SV40 early region promoter. *J. Mol. Appl. Genet.* 1 (1982), 327–41. PMID: 6286831.

[261] H. Heller et al.: Chromosomal insertion of foreign (adenovirus type 12, plasmid, or bacteriophage lambda) DNA is associated with enhanced methylation of cellular DNA segments. *Proc. Natl. Acad. Sci. U. S. A.* 92 (1995), 5515–9. PMID: 7777540.

[262] Z. Wang et al.: Detection of integration of plasmid DNA into host genomic DNA following intramuscular injection and electroporation. *Gene Ther.* 11 (2004), 711–21. PMID: 14724672.

[263] N. Van de Water et al.: A 20.7 kb deletion within the factor VIII gene associated with LINE-1 element insertion. *Thromb. Haemost.* 79 (1998), 938–42. PMID: 9609225.

[264] K. Müller et al.: Foreign DNA integration. Genome-wide perturbations of methylation and transcription in the recipient genomes. *J. Biol. Chem.* 276 (2001), 14271–8. PMID: 11278495.

[265] F. J. T. Staal et al.: Sola dosis facit venenum. Leukemia in gene therapy trials: a question of vectors, inserts and dosage? *Leukemia* 22 (2008), 1849–1852. PMID: 18769449.

[266] S. Hacein-Bey-Abina et al.: Insertional oncogenesis in 4 patients after retrovirus-mediated gene therapy of SCID-X1. *J. Clin. Invest.* 118 (2008), 3132–42. PMID: 18688285.

[267] R. Sipehia and G. Martucci: High-efficiency transformation of human endothelial cells by Apo E-mediated transfection with plasmid DNA. *Biochem. Biophys. Res. Commun.* 214 (1995), 206–11. PMID: 7669041.

[268] M. Takahashi et al.: Transformation of MC3T3-E1 cells following stress and transfection with pSV2neo plasmid. *Anticancer Res.* 22 (2002), 585–98. PMID: 12014626.

[269] C. H. Miao et al.: Long-term and therapeutic-level hepatic gene expression of human factor IX after naked plasmid transfer in vivo. *Mol. Ther.* 3 (2001), 947–57. PMID: 11407909.

[270] X. Ye et al.: Complete and sustained phenotypic correction of hemophilia B in mice following hepatic gene transfer of a high-expressing human factor IX plasmid. *J. Thromb. Haemost.* 1 (2003), 103–11. PMID: 12871546.

[271] A. Ehrhardt et al.: Episomal persistence of recombinant adenoviral vector genomes during the cell cycle in vivo. *J. Virol.* 77 (2003), 7689–95. PMID: 12805471.

[272] Y. Q. Li et al.: [The function of T7 promoter as cis-acting elements for polymerase II in eukaryotic cell]. *Yi Chuan Xue Bao* 27 (2000), 455–61. PMID: 10979193.

[273] A. C. on Immunization Practices: *ACIP Evidence to Recommendations for Use of Pfizer-BioNTech COVID-19 Vaccine*. 2021. URL: https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-etr.html.

[274] E. Mathieu et al.: A global database of COVID-19 vaccinations. *Nat. Hum. Behav.* 5 (2021), 947–953. PMID: 33972767.

[275] H. Cheng et al.: Efficacy and Safety of COVID-19 Vaccines in Phase III Trials: A Meta-Analysis. *Vaccines* 9 (2021). PMID: 34206032.

[276] H. Kouhpayeh and H. Ansari: Adverse events following COVID-19 vaccination: A systematic review and meta-analysis. *Int. Immunopharmacol.* 109 (2022), 108906. PMID: 35671640.

[277] J. Fraiman et al.: Serious Adverse Events of Special Interest Following mRNA Vaccination in Randomized Trials. *SSRN* (2022). URL: https://ssrn.com/abstract=4125239.

[278] Food and D. Administration: *Emergency Use Authorization for Pfizer-BioNTech COVID-19 Vaccine Review Memo*. 2020. URL: https://www.fda.gov/media/144416/download.

[279] H.-L. Wong et al.: Surveillance of COVID-19 vaccine safety among elderly persons aged 65 years and older. *Vaccine* 41 (2023), 532–539. PMID: 36496287.

[280] N. V. Center: *Search the VAERS Database*. 2023. URL: https://medalerts.org/vaersdb/index.php.

[281] E. Romero et al.: Safety of mRNA Vaccines Administered During the First Twenty-Four Months of the International COVID-19 Vaccination Program. *IJVTPR* 3 (2023), 891–910. DOI: 10.56098/ijvtpr.v3i1.70.

[282] D. Montano: Frequency and Associations of Adverse Reactions of COVID-19 Vaccines Reported to Pharmacovigilance Systems in the European Union and the United States. *Frontiers in public health* 9 (2022), 756633. PMID: 35186864.

[283] N. Barda et al.: Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. *N. Engl. J. Med.* 385 (2021), 1078–1090. PMID: 34432976.

[284] J. Montgomery et al.: Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military. *JAMA Cardiol.* 6 (2021), 1202–1206. PMID: 34185045.

[285] K. Jablonowski and B. S. Hooker: Delayed Vigilance: A comment on myocarditis in association with the COVID-19 injections. *IJVTPR* 2 (2022). DOI: 10.56098/ijvtpr.v2i2.61.

[286] Food and D. Administration: *Coronavirus (COVID-19) Update: FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Adolescents in Another Important Action in Fight Against Pandemic*. 2021. URL: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use.

[287] C. for Disease Control: *CDC Director Statement on Pfizer's Use of COVID-19 Vaccine in Adolescents Age 12 and Older*. 2021. URL: https://www.cdc.gov/media/releases/2021/s0512-advisory-committee-signing.html.

[288] C. for Disease Control: *Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination*. 2021. URL: https://web.archive.org/web/20210623132215/https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html.

[289] M. E. Oster et al.: Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021. *JAMA* 327 (2022), 331–340. PMID: 35076665.

[290] M. Li et al.: Myocarditis and Pericarditis following COVID-19 Vaccination: Inequalities in Age and Vaccine Types. *J. Pers. Med.* 11 (2021). PMID: 34834458.

[291] W. Straus et al.: Analysis of Myocarditis Among 252 Million mRNA-1273 Recipients Worldwide. *Clin. Infect. Dis.* 76 (2023), e544–e552. PMID: 35666513.

[292] G. Witberg et al.: Myocarditis after Covid-19 Vaccination in a Large Health Care Organization. *N. Engl. J. Med.* 385 (2021), 2132–2139. PMID: 34614329.

[293] A. Krug et al.: BNT162b2 Vaccine-Associated Myo/Pericarditis in Adolescents: A Stratified Risk-Benefit Analysis. *Eur. J. Clin. Invest.* 52 (2022), e13759. PMID: 35156705.

[294] G. T. Chua et al.: Epidemiology of Acute Myocarditis/Pericarditis in Hong Kong Adolescents Following Comirnaty Vaccination. *Clin. Infect. Dis.* 75 (2022), 673–681. PMID: 34849657.

[295] M. S. Kim et al.: Comparative safety of mRNA COVID-19 vaccines to influenza vaccines: A pharmacovigilance analysis using WHO international database. *J. Med. Virol.* 94 (2022), 1085–1095. PMID: 34709664.

[296] C. L. F. Sun et al.: Increased emergency cardiovascular events among under-40 population in Israel during vaccine rollout and third COVID-19 wave. *Sci. Rep.* 12 (2022), 6978. PMID: 35484304.

[297] Ø. Karlstad et al.: SARS-CoV-2 Vaccination and Myocarditis in a Nordic Cohort Study of 23 Million Residents. *JAMA Cardiol.* 7 (2022), 600–612. PMID: 35442390.

[298] D. Mevorach et al.: Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel. *N. Engl. J. Med.* 385 (2021), 2140–2149. PMID: 34614328.

[299] F. T. T. Lai et al.: Adverse events of special interest following the use of BNT162b2 in adolescents: a population-based retrospective cohort study. *Emerg. Microbes Infect.* 11 (2022), 885–893. PMID: 35254219.

[300] F. T. T. Lai et al.: Carditis After COVID-19 Vaccination With a Messenger RNA Vaccine and an Inactivated Virus Vaccine : A Case-Control Study. *Ann. Intern. Med.* 175 (2022), 362–370. PMID: 35073155.

[301] K. Goddard et al.: Risk of myocarditis and pericarditis following BNT162b2 and mRNA-1273 COVID-19 vaccination. *Vaccine* 40 (2022), 5153–5159. PMID: 35902278.

[302] A. Simone et al.: Acute myocarditis following a third dose of COVID-19 mRNA vaccination in adults. *Int. J. Cardiol.* 365 (2022), 41–43. PMID: 35870635.

[303] M. Massari et al.: Postmarketing active surveillance of myocarditis and pericarditis following vaccination with COVID-19 mRNA vaccines in persons aged 12 to 39 years in Italy: A multi-database, self-controlled case series study. *PLoS Med.* 19 (2022), e1004056. PMID: 35900992.

[304] M. Patone et al.: Risk of Myocarditis After Sequential Doses of COVID-19 Vaccine and SARS-CoV-2 Infection by Age and Sex. *Circulation* 146 (2022), 743–754. PMID: 35993236.

[305] stuff: *Myocarditis*. 2022. URL: https://my.clevelandclinic.org/health/diseases/22129-myocarditis.

[306] O. Tuvali et al.: The Incidence of Myocarditis and Pericarditis in Post COVID-19 Unvaccinated Patients-A Large Population-Based Study. *J. Clin. Med.* 11 (2022). PMID: 35456309.

[307] T. M. Tu et al.: Incidence of Cerebral Venous Thrombosis Following SARS-CoV-2 Infection vs mRNA SARS-CoV-2 Vaccination in Singapore. *JAMA network open* 5 (2022), e222940. PMID: 35297971.

[308] J. Hippisley-Cox et al.: Risk of thrombocytopenia and thromboembolism after covid-19 vaccination and SARS-CoV-2 positive testing: self-controlled case series study. *BMJ* 374 (2021), n1931. PMID: 34446426.

[309] J. D. Berild et al.: Analysis of Thromboembolic and Thrombocytopenic Events After the AZD1222, BNT162b2, and MRNA-1273 COVID-19 Vaccines in 3 Nordic Countries. *JAMA network open* 5 (2022), e2217375. PMID: 35699955.

[310] S. Dutta et al.: Analysis of Neurological Adverse Events Reported in VigiBase From COVID-19 Vaccines. *Cureus* 14 (2022), e21376. PMID: 35198288.

[311] R. Hosseini and N. Askari: A review of neurological side effects of COVID-19 vaccination. *Eur. J. Med. Res.* 28 (2023), 102. PMID: 36841774.

[312] M. Patone et al.: Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. *Nat. Med.* 27 (2021), 2144–2153. PMID: 34697502.

[313] K. Sato et al.: Facial nerve palsy following the administration of COVID-19 mRNA vaccines: analysis of a self-reporting database. *Int. J. Infect. Dis.* 111 (2021), 310–312. PMID: 34492394.

[314] R. Shibli et al.: Association between vaccination with the BNT162b2 mRNA COVID-19 vaccine and Bell's palsy: a population-based study. *The Lancet regional health. Europe* 11 (2021), 100236. PMID: 34751262.

[315] Anonymous: *Prednisone*. 2023. URL: https://www.sciencedirect.com/topics/medicine-and-dentistry/prednisone.

[316] E. Y. F. Wan et al.: Messenger RNA Coronavirus Disease 2019 (COVID-19) Vaccination With BNT162b2 Increased Risk of Bell's Palsy: A Nested Case-Control and Self-Controlled Case Series Study. *Clin. Infect. Dis.* 76 (2023), e291–e298. PMID: 35675702.

[317] Y.-H. Lai et al.: Peripheral Nervous System Adverse Events after the Administration of mRNA Vaccines: A Systematic Review and Meta-Analysis of Large-Scale Studies. *Vaccines* 10 (2022). PMID: 36560584.

[318] Y. Yanir et al.: Association Between the BNT162b2 Messenger RNA COVID-19 Vaccine and the Risk of Sudden Sensorineural Hearing Loss. *JAMA Otolaryngol. Head Neck Surg.* 148 (2022), 299–306. PMID: 35201275.

[319] M. Hertel et al.: Real-world evidence from over one million COVID-19 vaccinations is consistent with reactivation of the varicella-zoster virus. *J. Eur. Acad. Dermatol. Venereol.* 36 (2022), 1342–1348. PMID: 35470920.

[320] E. Y. F. Wan et al.: Herpes zoster related hospitalization after inactivated (CoronaVac) and mRNA (BNT162b2) SARS-CoV-2 vaccination: A self-controlled case series and nested case-control study. *Lancet Reg. Health West. Pac.* 21 (2022), 100393. PMID: 35128500.

[321] F. P. Polack et al.: Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N. Engl. J. Med.* 383 (2020), 2603–2615. DOI: 10.1056/nejmoa2034577.

[322] L. R. Baden et al.: Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N. Engl. J. Med.* 384 (2021), 403–416. PMID: 33378609.

[323] *To Evaluate the Safety, Tolerability, and Immunogenicity of BNT162b2 Against COVID-19 in Healthy Pregnant Women 18 Years of Age and Older*. 2022. URL: https://clinicaltrials.gov/ct2/show/NCT04754594.

[324] M. Demasi: *Whatever happened to Pfizer's covid vaccine trial in pregnant women?* 2023. URL: https://maryannedemasi.substack.com/p/exclusive-whatever-happened-to-pfizers.

[325] P. Inc.: *Comirnaty package insert*. 2022. URL: https://www.fda.gov/media/154834/download.

[326] M. Inc.: *Spikevax package insert*. 2022. URL: https://www.fda.gov/media/155675/download.

[327] C. for Disease Control: *Covid-19 Vaccines While Pregnant or Breast-feeding*. 2022. URL: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/pregnancy.html.

[328] U. Government: *Coronavirus vaccine—summary of Yellow Card reporting*. 2023. URL: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting.

[329] J. A. Thorp et al.: COVID-19 Vaccines: The Impact on Pregnancy Outcomes and Menstrual Function. *J. Am. Phys. Surg.* 28 (0), 28–34.

[330] VAERS interface at CDC WONDER: *Data as of April 7, 2023, retrieved using search terms "Infertility" and "Spontaneous Abortion" for "COVID-19 Vaccine" and "All Vaccine Products" in "All Territories."* 2023. URL: https://wonder.cdc.gov/vaers.html.

[331] A. Mascolo et al.: Maternal, fetal and neonatal outcomes among pregnant women receiving COVID-19 vaccination: The preg-co-vax study. *Front. Immunol.* 13 (2022), 965171. PMID: 36263025.

[332] K. M. N. Lee et al.: Investigating trends in those who experience menstrual bleeding changes after SARS-CoV-2 vaccination. *Sci. Adv.* 8 (2022). DOI: 10.1126/sciadv.abm7201.

[333] T. Parotto et al.: COVID-19 and the surge in Decidual Cast Shedding. *The Gazette of Medical Sciences* 3 (2022), 107–117. DOI: 10.46766/thegms.pubheal.22041401.

[334] M. DeSilva et al.: Evaluation of Acute Adverse Events after Covid-19 Vaccination during Pregnancy. *N. Engl. J. Med.* 387 (2022), 187–189. PMID: 35731916.

[335] M. Sadarangani et al.: Safety of COVID-19 vaccines in pregnancy: a Canadian National Vaccine Safety (CANVAS) network cohort study. *Lancet Infect. Dis.* 22 (2022), 1553–1564. PMID: 35964614.

[336] A. Dick et al.: Safety of SARS-CoV-2 vaccination during pregnancy-obstetric outcomes from a large cohort study. *BMC Pregnancy Childbirth* 22 (2022), 166. PMID: 35227233.

[337] A. Dick et al.: Safety of third SARS-CoV-2 vaccine (booster dose) during pregnancy. *Am. J. Obstet. Gynecol.* 4 (2022), 100637. PMID: 35398583.

[338] I. Gat et al.: Covid-19 vaccination BNT162b2 temporarily impairs semen concentration and total motile count among semen donors. *Andrology* (2022). PMID: 35713410.

[339] C. for Disease Control: *Ensuring COVID-19 Vaccine Safety in the US.* 2022. URL: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html.

[340] P. Duesberg: *Infectious AIDS: Have We Been Misled?* North Atlantic Books, 1995. URL: https://www.duesberg.com/books/pdbinfaids.html.

[341] P. Duesberg: *Inventing the AIDS Virus.* Regnery Publishing, 1996. URL: https://www.researchgate.net/publication/261948355_Inventing_the_AIDS_Virus.

[342] D. Rasnick: *Constant 1 million HIV+ in the USA 1986-2019.* 2019. URL: http://www.davidrasnick.com/aids/constant-one-million-hiv.html.

[343] D. J. DeNoon: *50,000 New HIV Infections Each Year in U.S.* 2011. URL: https://www.webmd.com/hiv-aids/news/20110803/50000-new-hiv-infections-each-year-in-us.

[344] J. Prejean et al.: Estimated HIV incidence in the United States, 2006-2009. *PLoS One* 6 (2011), e17502. PMID: 21826193.

[345] Anonymous: A cluster of Kaposi's sarcoma and Pneumocystis carinii pneumonia among homosexual male residents of Los Angeles and Orange Counties, California. *MMWR* 31 (1982), 305–7. PMID: 6811844.

[346] I. Young: *The Poppers Story: the Rise and Fall and Rise of the 'Gay Drug'*. 1995. URL: https://duesberg.com/articles/iypoppers.html.

[347] J. Lauritsen: *The AIDS war: propaganda, profiteering and genocide from the medical-industrial complex*. Asklepios, New York, 1993. URL: http://www.paganpressbooks.com/jpl/TAW-1.PDF.

[348] M. Chappelle: Book Review of "The AIDS War; Propaganda, profiteering, and genocide from the medical industrial complex" by John Lauritsen. *Bloomsbury Review* (1994). URL: https://www.paganpressbooks.com/TAWREV1.HTM.

[349] Anonymous: *HIV/AIDS Surveillance Report: U.S. HIV and AIDS cases reported through December 1997*. 1997. URL: https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-1997-vol-9-2.pdf.

[350] D. Rasnick: *Is AIDS or even HIV Sexually Transmitted? Debate in the BMJ & JAIDS 2001-2004*. 2005. URL: https://archive.org/details/rasnick-2005.

[351] M. Guliyev et al.: Human endogenous retrovirus-H insertion screening. *Mol. Med. Rep.* 7 (2013), 1305–9. PMID: 23358623.

[352] N. S. Padian et al.: Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: results from a ten-year study. *Am. J. Epidemiol.* 146 (1997), 350–7. PMID: 9270414.

[353] D. Gisselquist et al.: HIV infections in sub-Saharan Africa not explained by sexual or vertical transmission. *Int. J. STD AIDS* 13 (2002), 657–66. PMID: 12396534.

[354] J. A. Jacquez et al.: Role of the primary infection in epidemics of HIV infection in gay cohorts. *J. Acquir. Immune Defic. Syndr. 1988* 7 (1994), 1169–84. PMID: 7932084.

[355] R. Root-Bernstein: *Rethinking AIDS: the tagic cost of premature consensus*. The Free Press/Macmillan, 1993. URL: http://www.duesberg.com/subject/rrbbrethink.html.

[356] H. Miller et al.: *AIDS: The Second Decade*. National Academies Press (US), 1990. PMID: 25144007.

[357] S. Barton et al.: HTLV-III antibody in prostitutes. *Lancet* 326 (1985), 1424. PMID: 2867414.

[358] S. Day et al.: Prostitute women and public health. *BMJ* 297 (1988), 1585. PMID: 3147086.

[359] K. C. Hyams et al.: HIV infection in a non-drug abusing prostitute population. *Scand J Infect Dis* 21 (1989), 353–4. PMID: 2756346.

[360] W. Kopp and E. Dangl-Erlach: [HTLV-III monitoring in prostitutes in Vienna]. *Wien. Klin. Wochenschr.* 98 (1986), 695–8. PMID: 3466478.

[361] R. Lüthy et al.: Prevalence of HIV antibodies among prostitutes in Zürich, Switzerland. *Klin. Wochenschr.* 65 (1987), 287–8. PMID: 3495694.

[362] E. Burkett: *Is HIV guilty?* 1990. URL: https://archive.org/details/burkett-1990.

[363] N. Hodgkinson: *AIDS: can we be positive?* 1992. URL: https://archive.org/details/hodgkinson-1992.

[364] P. Pradhan et al.: Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag. *bioRxiv* (2020). DOI: 10.1101/2020.01.30.927871.

[365] C. McGovern: *Nobel Prize winner: Mass COVID vaccination an 'unacceptable mistake'*. 2021. URL: https://www.lifesitenews.com/news/nobel-prize-winner-mass-covid-vaccination-an-unacceptable-mistake-that-is-creating-the-variants/.

[366] C. Kline: *Department of Health & Human Servcies / Media Alert*. 1987. URL: http://www.duesberg.com/about/hhsalert.html.

[367] P. H. Duesberg: Retroviruses as carcinogens and pathogens: expectations and reality. *Cancer Res.* 47 (1987), 1199–220. PMID: 3028606.

[368] Anonymous: *WHO Workshop on AIDS in Central Africa; Bangui, Central African Republic 22 To 25 October 1985*. 1985. URL: https://archive-org/details/who-1985.

[369] D. Rasnick and C. Fiala: *But—what about Africa?* 2003. URL: https://www.altheal.org/statistics/africar&f.htm.

[370] D. Rasnick and C. Fiala: *But—what about Africa? Update (2006)*. 2006. URL: https://archive.org/details/rasnick-2006.

[371] Anonymous: *Uganda Population and Housing Census 2002*. 2002. URL: https://www.parliament.go.ug/cmis/browser?id=73df60ae-3c3b-459c-a315-292c4f9d600b%3B1.0.

[372] Anonymous: Global situation of the HIV/AIDS pandemic, end 2001. Part I. *Wkly Epidemiol Rec* 76 (2001), 381–6. PMID: 11775288.

[373] Anonymous: *Presidential AIDS Advisory Panel Report*. 2001. URL: https://archive.org/details/presidential-2001.

[374] P. H. Duesberg et al.: AIDS since 1984: no evidence for a new, viral epidemic–not even in Africa. *Ital. J. Anat. Embryol.* 116 (2011), 73–92. PMID: 22303636.

[375] Anonymous: The Durban Declaration. *Nature* 406 (2000), 15–6. PMID: 10894520.

[376] S. Mhlongo et al.: HIV a sexually transmitted disease? An analysis of the latest antenatal screening for HIV and syphilis from South Africa. *Int. J. STD AIDS* 14 (2003), 574–6. PMID: 12935393.

[377] Anonymous: *Report / National HIV and Syphilis Prevalence Survey South Africa 2006*. 2006. URL: https://archive.org/details/south-africa-2006.